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INDEX

TO

The New England Journal of Medicine

Volume 227, July 2, 1942 to December 31, 1942

PAGES ACCORDING TO WEEKLY ISSUES

PAGES	No	DATE	PAGES	No	DATE
1-38	1	July 2	499-522	14	Oct 1
39-86	2	July 9	523-574	15	Oct 8
87-120	3	July 16	575-616	16	Oct 15
121-158	4	July 23	617-652	17	Oct 22
159-202	5	July 30	653-690		Oct 29
203-240	6	Aug 6	691-726		Nov 5
241-276	7	Aug 13	727-770		Nov 12
277-324	8	Aug 20	771-812	21	Nov 19
325-362	9	Aug 27	813-856	22	Nov 26
363-394	10	Sept 3	857-897	23	Dec 3
395-426	11	Sept 10	898-938	24	Dec 10
427-464	12	Sept 17	939-974	25	Dec 17
465-494	13	Sept 24	975-1012	26	Dec 24
			1013-1058	27	Dec 31

BOOK REVIEWERS*

BALLARD, JAMES F
BROWN, E A
BUCK, ROBERT W
DAMESHEK, WILLIAM
DOWNING, JOHN G
GOLDBERG, BERNARD I
GREEN, ROBERT M
HARE, HUGH F
HINES, NORMAN E
KINGSLAND, L C

KUHNS, JOHN G
LILLY, ROLF
LOMBARD, HERBERT I
LYON, ARTHUR BATES
MANSTFIELD, JAMES S
MARKS, JOSEPH H
MC CARTHY, FRANCIS P
MOORE, MERRILL
O'HARA, DWIGHT
PAINTER, CHARLES F

PHANEUF, LOUIS E
RESNIK, JOSEPH
SAVITZ, HARRY A
SOSMAN, MERRILL C
SPECTOR, BENJAMIN
STONE, MOSES J
TAYLOR, GRANTLEY W
VIETS, HENRY R
WAITE, J HERBERT
WHITE, PAUL D

*This list includes only those whose work appears in this time

KEY TO ABBREVIATIONS

c — correspondence
cr — case record
e — editorial

MMS — Massachusetts Medical Society
me — medical opinion
mr — meeting report

misc — miscellaneous
n — notice
o — obituary

* — original article

SUBJECT INDEX

A

- ABSCESS, subdural: a clinicopathologic study [Kubik & Adams] 36—mr
- ADENOCARCINOMA of colon, with jejunocolic fistula [Schatzki & others] 885—cr
- Admiral of the Ocean Sea* (See Sinister Shepherd) 31—c
- ADRENALIN in base suspended in aqueous solution of sodium thioglycolate in treatment of asthma [Naterman] *736
- AGED (See Eczema and pruritus in aged) [Anderson] *653
- AGED DISEASES 853—misc
(See Skin)
- ALBUMINURIA and associated renal changes [Dock] 201—mr
in diagnostic value of serial measurements of ambulatory patients [Derow] *827
- ALCOHOL and cerebral vasodilatation [Loman & Myerson] *439
- ALLERGIC states in selectees, diagnosis of [Hyde] *241
- AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, Feb. 13, 690—n
- AMERICAN BOARD OF OPHTHALMOLOGY 361—n
- AMERICAN MEDICAL ASSOCIATION, annual meeting of, 81—c
(1943 meeting canceled) 527—MMS
- AMPULLA of Vater, papillary adenocarcinoma of [Adams & others] 265—cr
- ANEMIA, hypochromic, with koilonychia (spoon nails) [Clarke] *338
myeloid metaplasia of spleen with acute hemolytic [Brewster & Wollenman] *822
- ANESTHESIA, regional [Brown & Nicholson] *636
- ANEURYSM [Harwood] 681—cr
dissecting, of aorta, with rupture into mediastinum and left pleural cavity [Richardson & others] 712—cr
intracranial, of internal carotid artery [Botsford] *657
- ANKLE, tuberculosis of, in adults and children [Wasser sug] *436
- ANNOUNCEMENT, Viets, Henry R. 652—n
- AORTA aneurysm [Dieuaide & others] 603—cr
aneurysm [Harwood] 681—cr
coarctation of [Walker] 120—c
dissecting aneurysm of, with rupture into mediastinum and left pleural cavity [Richardson & others] 712—cr
stenosis [White & others] 927—cr
- APPENDICITIS, acute gangrenous, with rupture into root of mesentery [Brailey & others] 645—cr
healing [Franseen & others] 715—cr
- APPENDIX, primary carcinoma of, associated with acute appendicitis [Young & Wyman] *703
- ARGYLL ROBERTSON pupil 491—mc
- ARMY camps, communicable diseases in [Stokes] 237—mr
physician prepares to enter [Zollinger & Freedman] *370
- ARMY-NAVY "E" AWARD to Winthrop Chemical Company 1058—misc
- ARTHRITIS (See Knee contractures) [Kuhns] *975
rheumatoid, associated with splenomegaly and leukopenia [Talkov & others] *395
rheumatoid, treatment of [Short & Bauer] *442
- ASCORBIC acid deficiency associated with gastric lesions [Lund] *247
- ASTHMA, bronchial, use of ether in oil intramuscularly in treatment of [Maietta] *985
therapy [Naterman] *736; [Maietta] *985

- ATELECTASIS, congenital alveolar [Williams & others] 516—cr
- ATHEROSCLEROSIS [Leary] 573—mr
- AUDIOMETRY in general practice [Mueller] *617

B

- BACTEREMIA, hemolytic streptococcus [Rantz & Kirby] *730
- BACTERIOLOGICAL Laboratory of Health Department City of Boston 652—n
- BACTERIOLOGY of wounds of compound fractures of skull [Munro] *939
- BALLARD, JAMES F. (See Semicentennial) 610—c
- BASCH, WILLIAM E. R. (See Deprivation of license) 726—c
- BASE HOSPITALS 768
- BASILAR artery, thrombosis of [Kubik & others] 844—cr
- BILE pigments [Watson] 665, *705
- BILIARY-TRACT diagnosis *470
disease, significance of carotid-sinus reflex in [Engel & Engel] *470
surgery (See Rubber tube in biliary tract, retention of) *545
- BIOPSIES, renal, from hypertensive patients [Castleman] 37—mr
- BIRTH CONTROL (See Approaching referendum) 652—c
- BLOOD tests, approved laboratories for premarital [Jakmauh] 571—c
vessel aneurysm [Dieuaide & others] 603—cr
- BLUE SHIELD 197, 806—c
[Greene] 892—c
- BONE cyst, left humerus [Daland & others] 194—cr
device for internal fixation of [Smith] *510
diseases [Mallory] *955
granuloma [Green & others] 840—cr
- BOOK REVIEWS
(Maude) *Abbott: A memoir* [MacDermot] 498
Admiral of the Ocean Sea (See "Sinister Shepherd") [Morison] 31—c
Advancing Front of Medicine [Gray] 361
Allergy in Clinical Practice 361
Amor, A. J. 496
Angyal, A. 496
Anoxia: Its effect on body [van Liere] 892
Arthritis in Modern Practice [Steinbrocker & Kuhns] 770
Association for Research in Nervous and Mental Disease Vol. xxi 498
Atkinson, M. 276
Baker Memorial [Emerson] 202
Behind Mask of Medicine [Atkinson] 276
Bibliography of Aviation Medicine [Hoff & Fulton] 938
Biology of the Laboratory Mouse 202
Biological Symposia 614
Body Mechanics in Health and Disease [Goldthwait & others] 158
Brekhus, P. J. 616
Brinton, D. 496
Brown, L. 202
Brown, L. T. 158
Caldwell, J. A. 497
(*Edith*) *Cavell* [Judson] 158
Cerebrospinal Fever [Brinton] 496
Chinese Lessons to Western Medicine [Snapper] 498
Civilian Health in Wartime [Dieuaide] 938
Cohen, M. B. 532

- Communicable Disease Nursing* [Lynch] 498
(From) Cretin to Genius [Voronoff] 615
 Crossen, H S 361
 Crossen, R J 361
 Davis, L 532
 Dexter, L 615
 Diemaid, F R 938
Directory of Medical Specialists Certified by American Boards, 1942 616
Diseases of Blood and Atlas of Hematology [Kracke] 324
Diseases of Nervous System [Walshe] 616
Diseases of Women [Crossen & Crossen] 361
 Drinker, C K 892
 Emerson, H 202
Essentials of General Surgery [Ritchie] 240
Essentials of Occupational Diseases [Reed & Harecourt] 38
Eye Hazards in Industry [Resnick] 324
 Flexner, J T 152-c
 Flexner, S 152-c
Foundation for Science of Personality [Angyal] 496
 Freeman W 614
 Friedberg, C K 239
 Fulton, J F 938
Furtherance of Medical Research [Gregg] 497
 Goldswort, J E 158
 Gorsch R V 532
 Gray, G W 361
 Gregg, A 497
Guides to Therapy for Medical Officers 720-c
Gynecology and Female Endocrinology [Novak] 1058
 Harecourt, A K 38
 Harworth, N A 38
History and Evolution of Surgical Instruments [Thompson] 812
 Hoff, E C 938
 Holmes, G W 38
 Ilgenfritz, H C 240
Immunology [Sherwood] 616
 Jessner, L 158
 Joki, F 201
 Jordan, H H 496
 Judson, H 158
 Kahn, F 770
 Kelly, J F 812
 King E S J 323
 Korzybski, A 856
 Kracke, R R 324
 Kuhns, J G 158
 Kuntz, A 498
Lane Medical Lectures [Drinker] 892
 Libman, E 239
 Lichtwitz, L 532
 Lynch, T I 498
 MacDermot, H E 498
 MacDonald, E M 38
Manual of Allergy for General Practitioners [Cohen] 532
Manual of Pharmacology, with Its Applications to Therapeutics and Toxicology [Sollmann] 498
Manual of Treatment of Fractures [Caldwell] 497
 McCann L. 323
 McNeill, C 86
 Meekins, J C 324
Medical Aspect of Boxing [Joki] 201
 Mettler, F A 574
 Morison, S E 31-c
Nephritis [Lichtwitz] 532
Neuroanatomy [Mettler] 574
1941 Year Book of Industrial and Orthopedic Surgery 613
1941 Year Book of Pathology and Immunology 613
1941 Year Book of Public Health 497
Nostradamus The Man Who Saw Through Time [McCann] 323
 Novak, E 1058
Nutritional Deficiencies Diagnosis and treatment [Youmans & Patton] 770
 Nyswander, D B 1058
Our Sex Life A guide and counsellor for everyone [Kahn] 770
 Penick, R M, Jr 240
Perineoplastic Anatomy from Proctologist's Viewpoint [Gorsch] 532
 Polyak, S L 239
Primer on Prevention of Deformity in Childhood [Raney & Shands] 770
Principles of Neurological Surgery [Davis] 532
Preeclampsic and Eclampsic Toxemia of Pregnancy [Dexter & Weiss] 615
Psychosurgery [Freeman & Watts] 614
Rabies [Webster] 613
 Raney, R B 770
 Reed J V 38
 Resnick L 374
Retina [Polyak] 239
 Ritchie, W P 240
Roentgen Interpretation [Holmes & Ruggles] 38
Roentgen Technique [McNeill] 86
Roentgen Treatment of Infections [Kelly] 812
 Ruggles H E 38
 Ryan, V G 158
Science and Sanity [Korzybski] 856
 Sherwood N P 616
Shock Treatment in Psychiatry [Jessner & Ryan] 158
Sinister Shepherd (Admiral of the Ocean Sea) [Morison] 31-c
 Snapper I 498
 Sollmann T 498
Solving School Health Problems [Nyswander] 1058
 Steinbrocker, O 770
Story of Clinical Pulmonary Tuberculosis [Brown] 202
Subacute Bacterial Endocarditis [Libman & Friedberg] 239
Surgery of Heart [King] 323
Symptoms in Diagnosis [Meekins] 324
Synopsis of Preparation and Aftercare of Surgical Patients [Ilgenfritz & Penick] 240
 Swann, L T 158
Text Book of Human Anatomy [Kuntz] 498
Textbook of Surgery 498
Theory of Occupational Therapy [Haworth & MacDonald] 38
 Thompson, C J S 812
 van Lere, E J 892
 Voronoff S 615
 Walshe, F M R 616
War Department 974
 Watts J W 614
 Webster, L T 613
 Weiss, S 615
(William Henry) Welch and the Heroic Age of American Medicine [Flexner & Flexner] 152-c
Workmen's Compensation and Physician [Jordan] 496
X Ray Atlas of Silicons [Amor] 497
 Youmans, J B 770

- (Hugh) Young: *A surgeon's autobiography* 239
Your Teeth: Their past, present and probable future
 [Brekhus] 616
 BOSTON CITY HOSPITAL, May 5, 359; May 7, 426; May 12, 495; May 14, 528; 5th in series, 573—mr
 BOSTON CITY HOSPITAL HOUSE OFFICERS' ASSOCIATION 811—mr
 BOSTON GUILD FOR THE HARD OF HEARING, Work of [Pugh] *624
 BOSTON LYING-IN HOSPITAL JOURNAL CLUB, Apr. 15, 322—mr
 BOSTON MEDICAL LIBRARY—fuel oil 971—MMS
 (See Semicentennial) 610—e
 BOSTON ORTHOPEDIC CLUB, May 18, 529—mr
 BOSTON'S health units 1053—e
 BRAIN hematomas 115—e; [Munro] *87
 sulfonamide action on [Ingraham & Alexander] *374
 BREAST feeding 566—MMS
 BRONCHIECTASIS, cystic, of left upper lobe [Strieder & others] 996—cr
 BRONCHIOGENIC cyst [Adams & others] 560—cr
 BRONCHUS carcinoma of [Holmes] 503—MMS
 obstruction [Benedict] 1013—MMS
 tuberculosis [Benedict] 1013—MMS
 BURN THERAPY (See Burns)
 BURNS 355—e
 practical management of [MacCollum] 359—mr
 practical outline for treatment [MacCollum] *331
 therapy 85—mr
 BURSITIS, tuberculous [Klemperer & others] 762—cr
 (ROBERT) BURTON and His Drugs: The armamentarium of 1600 [Leonard] *216
 "BUSINESS as usual" 456—e

C

- CANCER [Nathanson] *830
 clinics [Simmons] 1011—MMS
 clinics, survey of state-aided [Simmons] 458—MMS
 of colon and rectum [Cattell] 494—mr
 of prostate, treatment of, with castration and administration of estrogen [Chute & Willets] *863
 report 462—MMS
 CANTEENS, Red Cross mobile 973
 CARCINOMA [Cass & others] 964—cr
 [Means & others] 799—cr
 (See Adenocarcinoma of colon) 885—cr
 (See Ampulla of Vater) 265—cr
 (See Liver-cell) 1000—cr
 of bronchus [Holmes] 503—MMS
 epidermoid, bronchiogenic, left lower lobe [King & others] 77—cr
 epidermoid, bronchiogenic, of right upper lobe [Pittman] 230—cr
 perforated, of sigmoid [Daland & others] 451—cr
 primary, of appendix associated with acute appendicitis [Young & Wyman] *703
 of prostate [Quinby] *512
 of prostate, castration for [Neusvanger & Vermooten] *626
 renal-cell (hypernephroma type), of right kidney [Barney & others] 521—cr
 of stomach [Michelsen] 111—cr
 of upper lobe bronchus of right lung with secondary abscess [Churchill & others] 22—cr
 CARDIOVASCULAR diagnosis, important clues in [White] *980
 CAROTID ARTERY, internal, intracranial aneurysm of [Botsford] *657

- CAROTID-SINUS reflex [Sigler] *725
 CESAREAN SECTION IN MASSACHUSETTS, 564—e
 in 1940 [DeNormandie] *121
 in 1941 [DeNormandie] *499
 five-year study of [DeNormandie] *533
 post-mortem, successful [Moran] *988
 CHILDBIRTH, hemorrhage in 889—MMS
 CHILD-GUIDANCE work, physician's status in [Solomon] *427
 CHILD MORTALITY (See Death rate in infancy and children) [McKay] 274—c
 CHILDREN in wartime, protection of [Smith] 236—mr
 CHOLANGIOGRAPHIC artifacts resembling common-duct stones [Clute & Lawrence] *727
 CHOLECYSTITIS, intrinsic diseases of liver simulating acute [Lawrence & Clute] *701
 CHRISTIAN, HENRY A. (See Note) 464—misc
 CHRISTMAS (See Pass the ammunition) 1005—e
 CHRISTMAS SEAL campaign 933—e
 CIRCULATORY stasis [Moritz] 855—mr
 CIVILIAN DEFENSE, 34, 84, 235, 273, 356, 425, 527, 768, 853, 890, 891, 936, 937, 973, 1011, 1057
 medical aspects of [Cutler] 86—mr
 CIVILIAN MEDICAL DEFENSE in Massachusetts [Cutler] 7—MMS
 COHN, EDWIN J. 120, 769—misc
 COLLEGE students, tuberculosis in 974—misc
 COLON, adenocarcinoma, with jejunocolic fistula [Schatzki & others] 885—cr
 cancer [Cattell] 494—mr
 COMMUNICABLE diseases in wartime 423—e
 respiratory diseases in wartime [Finland] 528—mr
 CONNECTICUT MEDICINE, heritage of 233—e
 CONSTITUTIONAL inadequacy 457—e
 CONTRACTS Massachusetts Medical Service 155
 CORPUS LUTEUM rupture [Foisie] *45
 CURRICULUM, medical 887—e

D

- DEATH rate in infancy and childhood 82—e
 [McKay] 274—c
 of x-ray pioneer 321—misc
 DEATHS
 Adams, Charles W. 723
 Blakely, David N. 651
 Bowers, Helen M. 464
 Briggs, Charles A. 1011
 Bryant, Alice G. 234
 Burnett, N. Lowe 235
 Cochran, William J. 890
 Coon, William H. 723
 Cotton, Curtis B. 688
 Dixon, Robert B. 1011
 Ellsworth, Samuel W. 936
 Faxon, William O. 852
 French, Ralph W. 973
 Frothingham, Charles B. 235
 George, Leslie H. 809
 Glidden, Howard K. 235
 Gorman, John W. 651
 Greenwood, Allen 723, 934
 Handy, Harry T. 612
 Harris, A. E. 155
 Hogan, Daniel J. 356
 Jack, Edwin E. 852, 933
 Jackson, Oliver H. 425, 464
 Jacoby, Rudolph 394
 Keeley, Thomas H. 890

- Kenealy, Joseph H 973
 La Marche, Walter J 32, 199
 Maguire, James A 273
 McBain, William H 273
 Metivier, Armand O 83
 Mikolaitis, Casimir J 570
 Morse, Almon G 235
 Olef, Isadore 1011
 O'Toole, John L 464
 Rowe, Arthur J 688
 Shults Frederick C 32
 Stack, Charles F 235
 Tuttle, George H 809
 Walker, Harry A 723
 Walsh, Charles J 464
 Watson, Francis S 1006—o
 Willoughby, Earle C 83
- DECONTAMINATION 84
 services 34
- EFFICIENCIES, dietary Therapy [Merrill] 85—c
- DELIVERY, operative, fatal 356—MMS
- DEPRIVATION of licenses [Gallupe] 528, 726, 892, 937—c
- DERMATOLOGY, military [Lane] *293
- DERMATOSES, occupational, recognition of [Lane] *39
- DETERIORATION of milk by bacterial growth under refrigeration at 40°F [Mott & Mazer] *174
- DIABETES Massachusetts Tuberculosis League 157—mr
 insipidus and pregnancy [Blotner & Kunkel] *287
 mellitus [Joslin & Root] *175
 mellitus, skin disturbances in [Rudy & Hoffmann] *893
- DIGITALIS, edema and diuretics [Freedberg & Blumgart] *874
- DIPHTHERIA carriers 970—c
- DISEASES (See Eczema and pruritus in aged) [Anderson] *653
 communicable, in army camps [Stokes] 237—mr
 communicable, in Massachusetts for June, 1942, résumé of 200, July, 356, Aug, 571, Sept, 810, Oct, 1057—misc
 in wartime, communicable 423—c
 in wartime, communicable respiratory [Finland] 528—mr
- DIURETICS, digitalis, edema and [Freedberg & Blumgart] *874
- DROWNING, blood changes [Jetter & Moritz] 894—mr
- DRUG therapy of migraine headache [Trowbridge & others] *699
- DRUGS and mental disease 318—c
 Robert Burton and his *The armamentarium of 1600* [Leonard] *216
- DUBOIS, RENE JULES 200—misc
- DUODENAL ULCER, chronic, active [Sweet & others] 267—cr
 perforation [Ulfelder & Allen] *780
 surgery *508
- DUPUYTREN'S contracture [Browne] 530—mr
- DURAL constricting ring with cervical protruded intervertebral disk [Haynes] *825

E

- ECHINOCOCCAL cysts [Jones & others] 759—cr
- ECLAMPSIA 972—MMS
 [Sewall] *281
 fetal 234—MMS
 toxemia and 1008—MMS
- ECZEMA and pruritus in aged [Anderson] *653
- EDEMA and diuretics, digitalis [Freedberg & Blumgart] *874

EDITORIALS

- American Medical Association, annual meeting of 81
 Boston's health units 1053
 Burns 355
 Business as usual 456
 Cesarean section in Massachusetts 564
 Christmas seal campaign 933
 Communicable diseases in wartime 423
 Constitutional inadequacy 457
 Death rate in infancy and childhood 82
 Diphtheria carriers 970
 Drugs and mental disease 318
 Eloquent sermon 610
 Fiftieth anniversary of Grenfell Mission 116
 Financial aid to needy medical students 423
 Gasoline and tire rationing 806
Guides to Therapy for Medical Officers 720
 Heritage of Connecticut medicine 233
 Hospitals and compulsory hospital insurance 969
 Industrial medicine in Massachusetts 391
 Industrial medicine for practitioners 198
 Institute on Industrial Medicine 649
 Instruction concerning treatment of gas casualties 850
 Instruction in industrial medicine 525
 Legal aspects of first aid 525
 Massachusetts Laboratory Technologists Reserve Corps 684
 Massachusetts Medical Service 197, 490, 806
 Medical Advisory Committee for Industrial Accident Board 271
 Medical curriculum 887
 National Hearing Week 649
 Naval Medical Officer Procurement 152, 684
The News 766
 1943, 1053
 Occupational skin disease 565
 One-day cure for syphilis 720
 Pan American medicine 355
 Pass the ammunition 1005
 Poliomyelitis research 1005
 Postconcussional syndrome 849
 Rehabilitation and prehabilitation 766
 Salvation Army appeal 490
 Semicentennial 610
 Senescent skin 684
 Shifting populations 271
 Significance of Rh factor 932
 Sinister Shepherd 31
 Spread of infantile paralysis 317
 Subdural hematomas 115
 Venereal disease control and pharmacist 888
 Virus, pneumonia and ornithosis 392
 War and Massachusetts physicians 30
 War and venereal disease 233
 (William Henry) Welch and the *Heroic Age of American Medicine* 152
- ELECTRIC-SHOCK therapy in mental disease, further experience with [Myerson] *403
- ELKIND, HENRY B (See Notes) 322—misc
- FLOQUENT section 610—c
- EMBOLISM 850—MMS
 in childbirth 807—MMS
- EMERGENCY medical service for a small city [Hill] *662
 relation of medicine to [Lahey] 1—MMS
- EMPHYSEMA, subdural [Grant & Kubik] 109—cr
- ENDOCARDITIS, subacute bacterial, mural [Richardson & others] 311—cr
- ENDOMETRIOSIS of uterus and sigmoid [McKittrick & others] 351—cr

- EPILEPSY, mebaral in treatment of [Cohen & Myerson] *336
 therapy (See Mebaral in treatment of epilepsy) [Cohen & Myerson] *336
- EPONYMS, MEDICAL
 Plaut-Vincent's angina 31
 Politzer bag 82
 Pott's disease 116
 Pott's fracture 154
 Profeta's law 199
 Purkinje fibers 234
 Queckenstedt maneuver 272
 Rauchfuss's triangle 319
 Raynaud's disease 356
 (Von) Recklinghausen's disease 393
 (Dorothy) Reed cells 424
 Riggs's disease 457
 (Argyll) Robertson pupil 491
 Roentgen ray 526
 Romberg's sign 566
 Rovsing's sign 611
 Sahli hemometer 650
 Scanzoni maneuver 685
 Schick test 721
 Schüller-Christian's disease 767
 Shiga-Flexner bacillus 807
 Sibson's groove 850
 Simmonds's disease 889
 Sims's position 934
 Sippy treatment 971
 Skodaic tympany 1008
 (Eustace) Smith sign 1054
- ERYTHEMA NODOSUM [Poppel & Melamed] *325
- ESSEX NORTH DISTRICT MEDICAL SOCIETY 687—MMS
- ESTROGEN, treatment of cancer of prostate with castration and administration of [Chute & Willets] *863
- EVANS MEMORIAL LECTURE, Mar. 27, 201—mr

F

- FACE and neck injuries [Wolfson] 573—mr
- FELTY'S SYNDROME [Willis] 769—c
- FEWKES, ERNEST E. (See Death of x-ray pioneer) 321—misc
- FIBRILLATION, paroxysmal auricular [Comeau] *134
- FILMS, medical (See Peptic ulcer film available) 464—misc
- FIRST AID, legal aspects of 525—c
 legal aspects of [Wells] 236—c
 physician's role in [Reggio] 10—MMS
- FITZ, REGINALD 236—misc
- FIXATION of bone, device for internal [Smith] *510
- FLUOROSCOPY, dangers associated with: diagnostic roentgenology [Schatzki] *18
- FOOT deformities [Cunningham] 572—c
 tuberculosis of, in adults and children [Wassersug] *436
- FRACTURES, civilian therapy [Bosworth] *95
 instruction of laymen in emergency splinting of [Bosworth] *95
 of skull, bacteriology of wounds of compound [Munro] *939

G

- GALL BLADDER, hydrops of [Linton & others] 229—cr
- GAS CASUALTIES instruction concerning treatment of 850—c

- instruction in diagnosis and treatment of 853
 therapy 850—c; 891, 937
- GASOLINE and tire rationing 806—c; 809
- GASTRODUODENOSTOMY in surgery of duodenal ulcer, place of [Clute & Sprague] *508
- GASTROINTESTINAL symptoms and inguinal hernia [Myers & Zollinger] *660
- GASTROSCOPY, clinical application of [McClure & Jankelson] *548
- GIBBS, FREDERIC A. 236—misc
- GLOMERULOSCLEROSIS, intercapillary, chronic, advanced [Urmy & others] 418—cr
- GONOCOCCAL infection in women and children, sulfonamide therapy in [Adair & Hac] *465
- GONORRHEA in women [Adair & Hac] *465
- GOVERNOR'S address [Blood] *787
- GREAT BRITAIN (See War Activities) 1011
- GREATER BOSTON MEDICAL SOCIETY, Apr. 7, 237—mr; Nov. 3, 690—n
- (ALLEN) GREENWOOD, resolutions on the death of 934—MMS
- GRENELL MISSION, fiftieth anniversary of 116—c
- GROVSTEIN, W. P. (See Deprivation of license) 892, 937—c
- Guides to Therapy for Medical Officers*, 720—c

H

- HALLORAN, ROY D. 464—misc
- HAND dissections [Flynn] 529—mr
 infections [Lyons] 530—mr; [Marble] 530—mr
 innervation of [Hamlin] 529—mr
 reconstruction [Bunnell] 531—mr
- HARVARD MEDICAL SCHOOL, appointments 235; 612—misc
 faculty promotions 200—misc
- HARVARD MEDICAL SOCIETY, Mar. 10, 85; Apr. 14, 275; Apr. 28, 573—mr
- (WILLIAM) HARVEY SOCIETY, May 8, 494; Sept. 25, 726—mr
- HEAD INJURIES, sequelae of war [Denny-Brown] 771, 813—MMS
- HEALING wounds [Holmes] *909
- HEALTH units, Boston's 1053—c
- HEARING handicaps in children of today: importance of clinic programs for their early study and remedial guidance [Guilder] *619
- HEARING, IMPAIRED
 Audiometry in general practice [Mueller] *617
 Hearing handicaps in children of today [Guilder] *619
 National Hearing Week 649—c
 Work of Boston Guild for Hard of Hearing [Pugh] *624
- HEART complications [Weyler & Dustin] *785
 disease (See Cardiovascular diagnosis) [White] *980
 disease, congenital [Bland & others] 1047—cr
- HEMATOMAS, cerebral subdural [Munro] *87
 subdural 115—c
- HEMATURIA, renal [Prather] *169
- HEMOGLOBIN carboxyl [Breyfogle] 856—mr
- HEMORRHAGE in childbirth 889—MMS
- HEFERNIA complications (See Gastrointestinal symptoms and inguinal hernia) [Myers & Zollinger] *660
- HERSEY, EARL G. (See Deprivation of license) 726—c
- HISTORY, MEDICAL
 (Robert) Burton and his drugs [Leonard] *216
 Heritage of Connecticut medicine 233—c
 Plaut-Vincent's angina 31—me
 Politzer bag 82—me

Pott's disease 116 — me
 Pott's fracture 154 — me
 Profeta's law 199 — me
 Purkinje filers 234 — me
 Queckenstedt maneuver 272 — me
 Rauchfuss's triangle 319 — me
 Rygnud's disease 356 — me
 (Von)Recklinghausen's disease 393 — me
 (Dorothy) Reed cells 124 — me
 Riggs's disease 457 — me
 Argyll Robertson pupil 491 — me
 Romberg's sign 566 — me
 Rossing's sign 611 — me
 Sahli hemometer 650 — me
 Scanzoni maneuver 685 — me
 Schick test 721 — me
 Schüller-Christurn's disease 767 — me
 Shiga-Flexner bacillus 807 — me
 Sibson's groove 850 — me
 Simmonds's disease 889 — me
 Sims's position 934 — me
 Sippy treatment 971 — me
 Skoduc tympany 1008
 (Eustace) Smith sign 1054 — me
 History, roentgenology (See Death of x ray pioneer)
 321 — misc

HOSPITAL preparedness [Wilinsky] 15 — MMS

HOSPITALS

Boston City Hospital, May 5, 359, May 7, 426, May 12, 495, May 14, 528, 5th in series 573 — mr
 and compulsory hospital insurance 969 — c
 Massachusetts General Hospital, Oct 27, 652 — n
 Massachusetts, national award to 689 — misc
 practice sessions for 936
 (Joseph H.) Pratt Diagnostic Hospital, medical conference program, Nov 3 27, 690 — n
 Humerus, bone cyst [Daland & others] 194 — cr
 HUNTINGTON TUMOR CLINIC [Faxon] 493 — c
 HYPERFUNCTION, simultaneous, of thyroid and parathyroid glands [Miller & Evans] *919
 HYPERNEPHROMA of left kidney, containing colon bacillus abscess [Quinby & others] 414 — cr
 HYPERPARATHYROIDISM [Lerman & others] 26 — cr
 HYPERPLASIA, megaloblastic, of bone marrow [Williams] 938 — mr
 HYPERTENSION, arterial [Wilkins] *104
 HYPERTHYROIDISM (See Massachusetts Memorial Hospital, six years' experience of thyroid service at) [Albright & Clute] *363

I

ILEUM tumors [Sowles, H K] 488 — cr
 IMMUNIZATION of adolescents, tetanus toxoid [Gallagher & others] *691
 of military personnel, present program for [Enders] *162
 INCOME limits determined for subscribers (See Massachusetts Medical Service) 117
 INDUSTRIAL ACCIDENT BOARD, medical advisory committee for 271 — c, [Toussaint] 274 — c
 INDUSTRIAL HEALTH 527 — MMS
 broadcasts 890
 Committee on 393 — MMS, [O'Hara & Muller] 572 — c
 and Postgraduate Instruction, Committee on (institute program) 650 — MMS
 and war [Lynch] 209 — MMS

INDUSTRIAL MROICINE, institute on 649 — c
 in Massachusetts 391 — c
 instruction in 525 — c
 for practitioners 198 — c
 INDUSTRIAL PHYSICIANS [O'Hara & Muller] 572 — c
 INDUSTRY, tuberculosis and 492 — misc
 INFANTILE PARALYSIS, spread of 317 — c
 INFLUENZA (See Pneumonia) *342
 INNER toe for undersized foot [Cunningham] 572 — c
 INSTITUTE ON INDUSTRIAL MEDICINE 649 — c
 INSURANCE, hospitals and compulsory hospital 969 — c
 INTERNSHIP, rotating [Philips] 810 — c
 INTERVERTEBRAL disk, dorsal constricting ring with cervical protruded [Haynes] *825
 IODINE, use of, to delineate a safety zone in rectum [Dittmore] *409

J

(EDWIN FRISBY) JACK 1863 1942 933 — o
 JOHNSON, A. L. ROY 892 — misc
 JOURNAL CLUB, Boston Lying in Hospital, Apr 15 322 — mr

K

KIDNEY carcinoma [Barney & others] 521 — cr
 cyst, solitary [Smith & others] 314 — cr
 disease [Fitz] *262
 hematuria [Prather] *169
 nephrosis [Beckman & others] 802 — cr, [Fremont Smith & others] 922 — cr
 pathology (See Proteinuria) 633
 tumors (See Hypernephroma of left kidney) 414
 KNEE, contractures, treatment of arthritis [Kulins] *975
 KOILONYCHIA (spoon nails), hypochromic anemia with [Clarke] *334
 KYPHOSCOLIOSIS, right dorsal, extreme [Glendy & others] 452 — cr

L

LAENNEC'S cirrhosis of liver [Williams] 938 — mr
 (WALTER JOSEPH) LAMARCHE, 1859 1942, 199 — o
 LAW and pathologist [Smith] 854 — mr
 (LEWIS CASS) LEDIARD JR., Fellowship 362 — n
 LEGAL aspects of first aid 525 — c
 LENIVALDO, LEO (See Deprivation of license) 528 — c
 LEUKEMIA, diagnosis of [Hamman] 275 — mr
 LEUKOPENIA, rheumatoid arthritis associated with splenomegaly and [Talkov & others] *395
 LICENSE (See Deprivation)
 suspension of [Gallup] 200 — c
 LIVER atrophy [Butler & others] 485 — cr
 LIVER CELL carcinoma, primary [Kranes & others] 1000 — cr
 cirrhosis [Urm] 75 — cr, [Breed & others] 677 — cr
 [Williams] 938 — mr
 diseases [Lawrence & Clute] *701
 echinococcal cysts of, and gastroduodenal omentum [Jones & others] 759 — cr
 function during sulfonamide therapy, plasma prothrombin and [Kapnick & others] *944
 LUNG carcinoma [Pittman] 230 — cr
 epidermoid carcinoma of [Cass & others] 964 — cr
 fibrosis in Raynaud's disease, observations concerning [Linenthal] *433
 LUPUS ERYTHEMATOSUS, acute disseminated, associated with finger lesions resembling lupus pernio [Downing & Messina] *408

- LYMPHOMA, MALIGNANT [Dieuaide & others] 642-cr
 [Breed & others] 881-cr
 lymphoblastic type, of ileum [Hamlin & others] 386-cr

M

- MALE sterility [Williams] *905
 MALPRACTICE INSURANCE (See Essex North District Medical Society) 687-MMS
 MASSACHUSETTS, cesarean section in 564-e; in 1940 [DeNormandie] 121; in 1941 [DeNormandie] 499; five-year study [DeNormandie] *533
 civilian medical defense in [Cutler] 7-MMS
 MASSACHUSETTS GENERAL HOSPITAL, Oct. 27, 652-n
 (See *The News*) 766-e
 MASSACHUSETTS hospitals, national award to 689-misc
 industrial medicine in 391-e
 MASSACHUSETTS LABORATORY TECHNOLOGISTS RESERVE CORPS 684-c; [Nickerson] 690-c
 MASSACHUSETTS MEDICAL SERVICE 83, 117, 155; 197-c; 490-e; 565; 806-e

MASSACHUSETTS MEDICAL SOCIETY

- American Medical Association 527
 Applicants for fellowship 566
 Bronchial obstruction and tracheobronchial tuberculosis [Benedict] 1013
 Cancer clinics, survey of state-aided 458; [Simmons] 1011
 Carcinoma of bronchus [Holmes] 503
 Civilian medical defense in Massachusetts [Cutler] 7
 Clinical application of gastroscopy [McClure & Jankelson] 548
 Committee on Industrial Health 199, 393; [O'Hara & Muller] 572

COMMITTEE ON MATERNAL WELFARE

- Analysis of causes of maternal death in Massachusetts during 1941, 611, 767
 embolism 807, 850
 heart disease 685
 hemorrhage 889, 935
 pneumonia 722
 sepsis 650
 surgical complications 1054
 toxemia and eclampsia 972, 1008

- Death following partial placenta separation and vaginal delivery 491
 Fatal anaphylactic shock resulting from pituitary extract 154
 Fatal eclampsia 234
 Fatal pernicious vomiting 425
 Fatal prenatal separation of placenta 32
 Gonococcal septicemia, pelvic peritonitis and thrombophlebitis 394
 Miscarriage followed by sepsis and death 272
 Operative delivery followed by shock and death 199, 356
 Plea for breast feeding 566
 Post-partum hemorrhage, followed by cerebral hemorrhage and death 527
 Post-partum shock followed by death 319
 Premature separation of placenta, followed by death 83
 Separation of placenta, complicated by chronic nephritis and hypertension 117
 Septicemia and death following internal podalic version 463

- Committees on Postgraduate Instruction and Industrial Health 527; (institute program) 650
 Council, proceedings of, Oct. 7, 743; proceedings of anniversary May 25-27, 54; stated meeting of, Oct. 7, 458
 Eczema and pruritus in aged [Anderson] 653
 Essex North District Medical Society (malpractice insurance) 687
 Five-year study of cesarean sections in Massachusetts [DeNormandie] 533
 Hospital preparedness [Wilinsky] 15
 Impact of war on venereal-disease problem [Vonderlehr] 203
 Industrial health and war [Lynch] 209
 Massachusetts public-health problems in wartime [Jakmauh] 206
 Medical-school plans for emergency [Avery] 13
 Nurses and war 1056
 Physician's role in first aid [Reggio] 10
 Practical outline for the treatment of burns [MacCollum] 331
 Present program for immunization of military personnel [Enders] 162
 Problem of certain tropical diseases in war [Meleney] 159
 Proceedings of Council, Oct. 7, 743
 Proceedings of one hundred and sixty-first anniversary May 25-27, 54
 Procurement and assignment service 1008
 for physicians in Massachusetts [Fitz] 2-MMS
 Relation of medicine to emergency [Lahey] 1
 Resolutions on death of Allen Greenwood 934
 Sequelae of war head injuries [Denny-Brown] 771, 813
 Society headquarters 971

SYMPOSIUM: MINOR PSYCHIATRIC DISTURBANCES IN WAR AND CIVILIAN LIFE

- Diagnosis of psychoneuroses [MacPherson] 575
 Psychiatric components in medical disease: psychosomatic medicine [Finesinger] 578
 Therapeutic procedures in psychoneurosis [Lindemann] 584

- Trauma of skin due to wartime activities [Downing] 539
 Tuberculosis increasing [Foley] 664
 World conflict and medical service [Pratt] 166

- MASSACHUSETTS medicine (See Cesarean sections in Massachusetts) [DeNormandie] in 1940, 121; in 1941, 499; five-year study, *533
 MASSACHUSETTS MEMORIAL HOSPITALS, six years' experience of thyroid service at [Albright & Clute] *363
 MASSACHUSETTS in 1940, cesarean section in [DeNormandie] *121
 in 1941, cesarean section in [DeNormandie] *499
 MASSACHUSETTS physicians, war and 30-e
 procurement and assignment service for physicians in [Fitz] 2-MMS
 MASSACHUSETTS PSYCHIATRIC SOCIETY, Nov. 9, 690-n
 MASSACHUSETTS public-health problems in wartime [Jakmauh] 206-MMS
 MASSACHUSETTS, résumé of communicable diseases in, June, 200; July, 356; Aug., 571; Sept., 810; Oct., 1057-misc
 MASSACHUSETTS SOCIETY FOR MENTAL HYGIENE 322-misc
 MASSACHUSETTS TUBERCULOSIS LEAGUE, Apr. 9, Diabetes Committee 157-mr
 MASSIVE hematuria of renal origin [Prather] *169

- MASTOIDECTOMY wounds, use of sulfadiazine in manage-
ment of simple [Tucker & Flake] *1021
- MATERNAL MORTALITY in Massachusetts 722, 1008,
1054—MMS
Embolism 807, 850—MMS
Heart disease 685—MMS
Hemorrhage 935—MMS
Hemorrhage in childbirth 889—MMS
Medical causes 767—MMS
Toxemia and eclampsia 972—MMS
- McCANN, JAMES C. (president) (See Massachusetts Med-
ical Service) 33
- MEDICAL in treatment of epilepsy [Cohen & Myerson]
*336
- MEDIASTINUM, fibroma of [Pittman & others] 557—cr
- MEDICAL EDUCATION of public [Grillagher] 811—c
- MEDICAL LIBRARY ASSOCIATION, May 79, 394—misc
- MEDICAL-SCHOOL plans for emergency [Avery] 13—MMS
- MEDICAL STUDENTS, financial aid to needy 423—c
- MEDICINE to emergency, relation of [Lahey] 1—MMS
- MENTAL disease, drugs and 318—c
disorders (See Electric-Shock therapy in mental dis-
ease, further experience with) [Myerson] *403
disorders—complications [Bell & others] *901
- MESENTERIC thrombosis in mentally ill patients [Bell &
others] *901
- MESENTERY tumors [Breed & others] 881—cr
- MIGRAINE HEADACHE, drug therapy of [Trowbridge &
others] *699
- MILITARY MEDICINE 911—mr
[Denny Brown] *771
(See Head injuries) 813—MMS
- MILK determination [Mutt & Mizer] *174
- MISCARRIAGE 272—MMS
- MORGAN, PHILIP M. (vice president) (See Massachusetts
Medical Service) 33
- MORTALITY, infantile 82—c
- MORTUARY service, plans for 1057
- MOSELEY, HARRIS P. 236—misc
- MUMPS, surgical treatment of severe orchitis in [Wessel-
hoeft & Vose] *277
- MYELOID metaplasia of spleen with acute hemolytic anemia
[Brewster & Wollmann] *822
- MYOCARDIAL INFARCTION, Premonitory symptoms of
[Boyer] *628
- N
- NAILS (See Anemia) *338
- NATIONAL award to Massachusetts hospitals 689—misc
Hearing Week 649—c
- NAVAL MEDICAL OFFICER PROCUREMENT 152, 694—c
[Palmer] 156, 689—c
- NAVAL RESERVE, enlistment in [Palmer] 425—c
- NEPHROSIS [Beckman & others] 802—cr
- NERVE BLOCK, intercostal [Starr & Gilman] *102
- NERVOUS-SYSTEM diseases Physical therapy [Watkins]
*48
virus infections [McFrit & Thomas] 358—mr
- NEW ENGLAND OPHTHALMIC AND GYNECOLOGICAL SOCIETY
937—misc
- NEW ENGLAND PATHOLOGICAL SOCIETY, Feb 19, 36, Mar
19, 854 May 23, 937—mr
- NEW ENGLAND PEDIATRIC SOCIETY, Mar 25, 236—mr
- NEW ENGLAND SECTION AMERICAN UROLOGICAL ASSOCIA-
TION
Circulation for carcinoma of prostate [Neuwanger &
Vermooten] 626
- Surgical treatment of severe orchitis in mumps [Wes-
selhoeft & Vose] 277
- URINARY typhoid carriers [Buddington & Gilman] 400
The News 766—c
- NEW ENGLAND SURGICAL SOCIETY
Ascorbic acid deficiency associated with gastric lesions
[Lund] 247
Bacteriology of wounds of compound fractures of skull
[Munro] 939
Cerebral subdural hematomas [Munro] 87
- NEW HAMPSHIRE MEDICAL SOCIETY
- DEATHS
- Cotton, C. B. 688
Rowe A. J. 688
Governor's address [Blood] 787
Important clues in cardiovascular diagnosis [White] 980
Proceedings of the One Hundred and Fifty First An-
nual Meeting May 11-13, 181, 300, 672
Sulfonamide therapy in gonococcal infection in women
and children [Adair & Hac] 465
- 1943, 1053—c
- NURSES and war [Lee] 1056—MMS
- NUTRITION Appearance of tongue as index of nutritional
deficiency [Jeghies] *221
- O
- OBJECTOR [Greene] 892—c
- OBSTETRICS contagious disease in relation to [Place] 322—mr
- OCCUPATIONAL diseases 119—misc
skin disease 565—c
- OPERATIVE technique surgical care and [Stewart] *480
- OPTIC chiasm, glioma of [Katzman & Williams] 938—mr
- ORCHITIS in mumps surgical treatment of severe [Wes-
selhoeft & Vose] *777
- ORCHITIS, virus pneumonia and 997—c
- ORTHOPEDIC surgery [Van Gorder] *737
- OSTIUM fibrous cysts [Aub & others] 190—cr
- OSTEOID osteoma second lumbar vertebra [Smith
Petersen] 143—cr
- OVARY cyst [Taylor & others] 1045—cr
- P
- PAN AMERICAN MEDICINE 375—c
- PANCREAS, carcinoma of body and tail of [Meuns & others]
793—cr
- PANCREATIC lithiasis clinical features of [Moss & Freis]
*590
- PANCREATITIS, acute hemorrhagic [Jones & others] 961—cr
- PARALYSIS (See Quinine methochloride treatment of spastic
children) [Press] *475
- PARASITIC disease prevalent in African and Pacific theaters
of war [Brown] 811—mr
- PARASITOID hyperfunction [Miller & Evans] *949
- PAROXYSMAL auricular fibrillation, mechanism for syncopal
attacks associated with [Comaru] *134
- PASS the immunization 1005—c
- PATHOLOGY Bone diseases [Mallory] *955
legal [Smith] 854—mr
- PENITENTIARY, chronic essential [Bowman & Beck] 938—mr
- PEPTIC ULCER film available 464—misc
- PERIPHERAL diseases [Powers] 612—c
vascular disease [Silbert] 237—mr
- PERITONITIS (See Duodenal ulcer) [Sweet & others]
267—cr
- PERSONNEL military Immunization [Enders] *162

- PHARMACIST, venereal disease control and 888—e; 891—misc
- PHARMACOLOGY and pharmacotherapy [Friedgood] *788
- PHYSICAL THERAPY for diseases of nervous system [Watkins] *48
- PHYSICIANS' political responsibility of [Landesman] 725—c
- PHYSICIAN'S role in first aid [Reggio] 10—MMS
- PHYSIOLOGY [Hoff] *136
- PITUITARY adenoma, chromophobic type [Reifenstein] 145—cr
extract shock 154—MMS
- PLACENTA, adherent 199—MMS
separation 32, 83, 117, 491—MMS
- PLASMA prothrombin and liver function during sulfonamide therapy [Kapnick & others] *944
- PLAUT-VINCENT'S angina 31—me
- PLEUROPERICARDIAL cyst [Lerman & others] 606—cr
- PLEUROPNEUMONIALIKE organisms from human patients, isolation of [Smith & Dienes] 36—mr
organisms, nature of [Dienes] 37—mr
- PLYMOUTH DISTRICT MEDICAL SOCIETY, Apr. 16, 158—mr
- PNEUMONIA, virus, and ornithosis 392—c
- PNEUMONIAS, VIRUS
I. Pneumonias associated with known nonbacterial agents: influenza, psittacosis and Q fever [Finland & Dingle] *342
II. Primary atypical pneumonias of unknown etiology [Dingle & Finland] *378
- POLIOMYELITIS research 1005—c
- POLITZER bag 82—me
- POPULATIONS, shifting 271—c
- POSTCONCUSSIONAL syndrome 849—c
- POSTGRADUATE instruction 527—MMS
- POSTPARTUM hemorrhage 527—MMS
- POTT'S DISEASE 116—me
- POTT'S FRACTURE 154—me
(JOSEPH H.) PRATT DIAGNOSTIC HOSPITAL, medical conference program, Nov. 3-27, 690—n
- PREGNANCY (See Toxemia and eclampsia) 1008—MMS
complications (See Diabetes insipidus and pregnancy) [Blotner & Kunkel] *287
(See Maternal mortality in Massachusetts) 972—MMS
paroxysmal tachycardia in [Weyler & Dustin] *785
- PREMARITAL blood tests, approved laboratories for [Jakmauh] 571—c
- PREOPERATIVE care [Cope & Welch] *870
- PROCUREMENT AND ASSIGNMENT SERVICE 118, 464, 491, 688, 723, 1008—MMS
(See Eloquent sermon) 610—c
Massachusetts physicians [Fitz] 2—MMS
(See War Activities) 688
- PROFETA'S LAW 199—me
- PROGRESS, MEDICAL
Arterial hypertension [Wilkins] 104
Bile pigments [Watson] 665, 705
Cancer [Nathanson] 830
Carcinoma of prostate [Quinby] 512
Diabetes mellitus [Joslin & Root] 175
Diagnostic roentgenology: dangers associated with fluoroscopy [Schatzki] 18
Digitalis, edema and diuretics [Freedberg & Blumgart] 874
Diseases of thyroid gland [Means] 594
Kidney disease [Fitz] 262
Military dermatology [Lane] 293
Nutrition: appearance of tongue as an index of nutritional deficiency [Jeghers] 221
Orthopedic surgery [Van Gorder] 737
Pathology: diseases of bone [Mallory] 955
Pharmacology and pharmacotherapy [Friedgood] 788
Physical therapy for diseases of nervous system [Watkins] 48
Physiology [Hoff] 136
Radiation therapy [Dresser] 410
Regional anesthesia [Brown & Nicholson] 636
Sulbestrol [Rock & Menkin] 552
Sulfonamides
I. Their mode of action and pharmacology [Janeway] 989
II. Their clinical use [Janeway] 1029
Surgical care and operative technic [Stewart] 480
Treatment of rheumatoid arthritis [Short & Bauer] 442
Virus pneumonias
I. Pneumonias associated with known nonbacterial agents; influenza, psittacosis and Q fever [Finland & Dingle] 342
II. Primary atypical pneumonias of unknown etiology [Dingle & Finland] 378
Wound healing [Holmes] 909
- PROSTATE, carcinoma of [Quinby] *512
castration for carcinoma of [Neuswanger & Vermooten] *626
treatment of cancer of, with castration and administration of estrogen [Chute & Willets] *863
- PROTEINURIA and associated renal changes [Dock] *633
- PRURITUS, eczema and, in aged [Anderson] *653
- PSITTACOSIS (See Pneumonias) *342
- PSORIASIS, treatment of, with sarsaparilla compound [Thurmon] *128
- PSYCHIATRIC components in medical diseases: psychosomatic medicine [Finesinger] *578
- PSYCHIATRY, practical, with adolescents [Sullivan & Billig] *253
- PSYCHONEUROSES, diagnosis of [MacPherson] *575
therapy [Landemann] *584
- PSYCHOSOMATIC medicine: psychiatric components in medical disease [Finesinger] *578
- PSYCHOTHERAPY technic [Sullivan & Billig] *253
- PUBLIC-HEALTH problems in wartime, Massachusetts [Jakmauh] 206—MMS
- PULMONARY fibrosis, relation of peripheral diseases to [Powers] 612—c
ventilation, effect of postoperative intercostal-nerve block on [Starr & Gilman] *102
- PURKINJE FIBERS 234—me
- PURPURA, thrombocytopenic, rare type of acute [Altschule] *477
- PUTREFACTION [Bequaert] 856—mr

Q

- Q FEVER (See Pneumonias) *342
- QUININE methochloride treatment of spastic children [Press] *475
- QUECKENSTEDT maneuver 272—me

R

- "RACE, Color and Religion" [Goldstein & O'Hara] 769—c
- RADIATION therapy [Dresser] *410
- RAUCHFUSS'S TRIANGLE 319—me
- RAYNAUD'S DISEASE 356—me
observations concerning pulmonary fibrosis in [Linenthal] *433

- Reader's Digest* (See Medical education of public)
[Gillagher] 811—c
(Von) RECKLINHAUSEN's disease 393—me
RECORDS, adequate clinical [Pruitt] *695
RECTAL cancer [Crittell] 494—mr
RECTUM use of iodine to delineate a safety zone in [Dit
more] *409
RED CROSS mobile canteens 973
(DOROTHY) REED cells 424—me
REHABILITATION and prehabilitation 766—c
RHE FACTOR, hemolytic transfusion reactions due to [Dia
mond] *857
significance of 932—c
REFERENDUM approaching [Robey & Ellis] 652—c
REFUGEE Physicians [Fischer] 157—c
RHUS TOXIN [Downing] 426—c
RIGGS's disease 457—me
(ARGYLL) ROBERTSON pupil 491—me
ROENTGEN ray 526—me
ray therapy [Wheatley] 158—mr
ROENTGENOLOGY diagnostic dangers associated with fluor
oscopy [Schatzki] *18
(See Death of x ray pioneer) 321—misc
ROSENBERG's sign 566—me
ROVINGS sign 611—me
RUBBER TUBE in biliary tract, retention of [Consales]
*545
RUSSELL, FREDERICK F 1058—misc

S

- SAHILI hemometer 650—me
SALEM TUMOR CLINIC, Oct 30, 725—misc
SALVATION ARMY appeal 490—c
SARSAPARILLA compound, treatment of psoriasis with
[Thurmon] *128
SCANZONI maneuver 685—me
SALIC test 721—me
SCHÜLLER-CRISTIAN's disease 767—me
SELECTIVE diagnosis of allergic states in [Hyde] *241
SELECTIVE SERVICE Registration (See Race, Color and Re
ligion) 769—c
SEMICENTENNIAL 610—c
SEMINAL fluid identification [Pollak] 855—mr
SEPTICEMIA 394—MMS
puerperal 463—MMS
SHIGA-FLEXNER bacillus 807—me
SHOCK, anaphylactic 154—MMS
post partum 319—MMS
SIBSON's groove 850—me
SIGMOID perforated carcinoma of [Daland & others]
451—c
SIMMONS's disease 889—me
Sims's test 934—me
'SINISTER SHEPHERD' 31—c
SIPPY treatment 971—me
SITUS INVERSUS, complete [Pasternack] *953
SKIN and diabetes mellitus [Rudy & Hoffmann] *893
disease occupational 565—c
disturbances in diabetes mellitus their relation to vita
min deficiencies [Rudy & Hoffmann] *893
senescent 684—c
trauma due to wartime activities [Downing] *539
SKODAE tympany 1008—me
SKULL fractures, bacteriology [Munro] *939
(EUSTACE) SMITH sign 1054—me
SOCIETIES
Boston Lying in Hospital Journal Club, Apr 15, 322—mr

- Boston Orthopedic Club, May 18, 529—mr
LSESS North District Medical Society 687—MMS
Greater Boston Medical Society, Apr 7, 237—mr,
Nov 3, 690—n
Harvard Medical Society, Mar 10, 85, Apr 14, 275,
Apr 29 573—mr
(William) HARVEY Society, May 8, 494, Sept 25, 726—mr
Massachusetts Psychiatric Society, Nov 9, 690—n
Massachusetts Tuberculosis League, Apr 9, 157—mr
Medical Library Association, May 79, 394—misc
New England Obstetrical and Gynecological Society
937—misc
New England Pathological Society, Feb 19, 36, Mar
19, 854 May 23, 937—mr
New England Pediatric Society, Mar 25, 236—mr
Plymouth District Medical Society, Apr 16, 158—mr
Suffolk District Medical Society, Apr 29, 358—mr
SPALDING, MANFORD R 200—c
SPANISH SPEAKING people, pulmonary tuberculosis among
724—misc
SPASTIC Therapy (See Quinine methochloride treatment
of spastic children) [Press] *475
SPLEEN, myeloid metaplasia of, with acute hemolytic ane
mia [Brewster & Wollenman] *822
SPLENOMEGALY and leukopenia, rheumatoid arthritis as
associated with [Talkov & others] *395
STATE MEDICINE [Blood] *787
STEAD, EUGENE A, JR 200—misc
STERILITY, male [Williams] *905
STIBESTROL [Rock & Menkin] *552
STOMACH carcinoma 111—c
diseases (See Ascorbic acid deficiency associated with
gastric lesions) [Lund] *247
ulcer perforation [Ulfelder & Allen] *780
STREPTOCOCCAL infection [Hurwitz & Prien] *46
STUDENT aid 423—c
SUFFOLK DISTRICT MEDICAL SOCIETY, Apr 29, 358—mr
SULFADIAZINE, use of, in management of simple mastoi
ectomy wounds [Tucker & Flake] *1021
SULFANILAMIDE for treatment of infection due to micro
aerophilic streptococci [Hurwitz & Prien] *46
SULFONAMIDE drugs, experimental application of, to
cerebral cortex [Ingraham & Alexander] *374
nephrosis [Fremont-Smith & others] 922—c
therapy in gonococcal infection in women and children
[Adair & Hae] *465
therapy, plasma prothrombin and liver function dur
ing [Kapnick & others] *944
SULTONAMIDES
I Their mode of action and pharmacology [Janeway]
*989
II Their clinical use [Janeway] *1029
SURGERY in pregnancy 1054—MMS
traumatic [Marble] 426—mr
SURGICAL care and operative technic [Stewart] *480
SYMPOSIUM MINOR PSYCHIATRIC DISTURBANCES IN WAR
AND CIVILIAN LIFE
Diagnosis of psychoneuroses [MacPherson] 575
Psychiatric components in medical disease psychoso
matic medicine [Finesinger] 578
Therapeutic Procedures in Psychoneurosis [Lindemann]
584
SYPHILIS [Breed & others] 677—c
(See Optic chiasm, gumma of) [Katzman & Williams]
938—mr
history (See 'Sinister Shepherd') 31—c
one day cure for 720—c [Gillagher] 811—c

T

- TACHYCARDIA, paroxysmal, in pregnancy [Weyler & Dustin] *785
 paroxysmal, phonocardiographic studies in case of [Weyler & Dustin] *733
- TESTOSTERONE, therapeutic evaluation of, in peripheral vascular disease, in [Beaser & Massell] *43
- TETANUS toxoid immunization of adolescents [Gallagher & others] *691
- THIGH synovium [Larson & others] 352 - cr
- THORACIC surgery [Churchill] 495 - mr
- THROMBOSIS of basilar artery [Kubik & others] 844 - cr
 recent, mesenteric and portal [Smithwick & others] 388 - cr
- THYROID diseases [Means] *594
 and parathyroid glands, simultaneous hyperfunction of [Miller & Evans] *949
- THYROIDECTOMY, care of patients requiring [Cope & Welch] *870
- TIRE rationing, gasoline and 806 - c; 809
- TONGUE (See Nutrition) [Jeghers] *221
- TOXEMIA 972 - MMS
 and eclampsia 1008 - MMS
- TRANSFUSION, hemolytic, reactions due to Rh factor: A preventable danger [Diamond] *857
- TROPICAL diseases in war, problem of certain [McLency] 159 - MMS
- TUBERCULOSIS, chronic miliary [Welch] *1025
 in college students 974 - misc
 of foot and ankle in adults and children [Wassersug] *436
 incidence 724 - misc; [Foley] 664 - MMS
 in industry 119, 492 - misc
 pulmonary, among Spanish-Speaking people 724 - misc
 tracheobronchial, bronchial obstruction and [Benedict] 1013 - MMS
 undiagnosed, in elderly persons 853 - misc
 work tolerance following 320 - misc
- TUBERCULOUS bursitis [Klemperer & others] 762 - cr
- TUFTS COLLEGE MEDICAL SCHOOL, gift of land 769 - misc
 scholarships 236 - misc
- TWOMEY, EDMUND L. (treasurer) (See Massachusetts Medical Service) 33
- TYPHOID carriers, urinary [Buddington & Gilman] *400
- TYPHOID FEVER [Goodman & others] 937 - mr

U

- ULCER perforation [Ulfelder & Allen] *780
- UNITED STATES CIVIL SERVICE EXAMINATION
 Junior medical officer
 psychiatric resident 240 - n
 rotating internship 240 - n
- UTERUS (See Endometriosis)

V

- VASCULAR disease, peripheral, therapeutic evaluation of testosterone in [Beaser & Massell] *43
- VASODILATATION, alcohol and cerebral [Loman & Myerson] *439
- VENEREAL-DISEASE control and pharmacist 888 - c; 891 - misc
 problem, impact of war on [Vonderlehr] 203 - MMS
 war and 233 - c

- VERTEBRA, osteoid osteoma 143 - cr
- VIRUS infections of nervous system [Merritt & Thomas] 358 - mr
- VITAMIN deficiencies (See Skin and diabetes mellitus) [Rudy & Hoffmann] *893
- VOMITING in pregnancy 425 - MMS

W

- WAR (See Allergic states in selectees, diagnosis of) [Hyde] *241
 (See Communicable diseases in army camps) [Stokes] 237 - mr
 (See Dermatology, military) [Lane] *293
 impact of, on venereal-disease problem [Vonderlehr] 203 - MMS
 industrial health and [Lynch] 209 - MMS
 and Massachusetts physicians 30 - c
 medicine (See Trauma of skin)
 morale (See "Business as usual") 456 - c
 nurses and [Lee] 1056 - MMS
 parasitic disease prevalent in African and Pacific theaters in [Brown] 811 - mr
 problem of certain tropical diseases in [McLency] *159
 (See Protection of children in wartime) [Smith] 236 - mr
 and venereal disease 233 - c
 (See "World Conflict and Medical Service") [Hayes et al] 357 - c
- WAR ACTIVITIES
 American Red Cross Expansion of blood-procurement project 320
 Civilian Defense
 Base hospitals, emergency 768
 Decontamination, aids to 84
 Decontamination services 34
 Emergency base hospitals 768
 Films, instructional 356
 Gas casualties therapy 937
 Industrial-health broadcasts 890
 Industrial plants, relation of emergency medical services to 235
 Instruction in diagnosis and treatment of gas casualties 853, 891
 Lessons from British experience in civil defense 1011
 Nurses' aides, OCD urges recruitment of more 273
 Plans for mortuary service 1057
 Practice sessions for hospitals 936
 Red Cross mobile canteens 973
 Supplies, conservation of dealers' stocks of medical and surgical 425
- Gas, how to protect yourself against 156
- Hospitals, supplemental staffs for emergency base 570
- Office of Price Administration gasoline and tire rationing 809
- Procurement and Assignment Service 464, 491, 688, 723
- Duties of various units 118
- Selective service 723
- WAR SERVICE
 (See Army, physician prepares to enter) [Zollinger & Freedman] *370
 Hospital preparedness [Wilinsky] 15 - MMS
 Medical-school plans for emergency [Avery] 13 - MMS
 and medicine [Pratt] 166 - MMS
 physicians 30 - c
 physicians in [Lahey] 1 - MMS

WARTIME activities, trauma of skin due to [Downing]
 •539
 communicable diseases in 423-c
 communicable respiratory diseases in [Finland] 528-mr
 Massachusetts public-health problems in [Jakmauh]
 206-MMS

WASIBURN, FRANK H. 322-misc
 (FRANCIS S.) WATSON, 1853-1942, 1006-o
 (WILLIAM HENRY) WELCH [Palmer] 275-c
 [Bartlett] 357-c
 and the *Heroic Age of American Medicine* 152-c
 (Dr.) WILINSKY's sixtieth birthday 1057-misc

WINTHROP CHEMICAL COMPANY, Army-Navy "E" award
 1058-misc
 WORLD CONFLICT and medical service [Pratt] 166-MMS
 and medical service [Hayes et al] 357-c
 WOUND healing [Holmes] •909

Y

YALE UNIVERSITY SCHOOL OF MEDICINE, Oct. 7-Dec. 23,
 362-n

Z

ZARCH (See Deprivation of licenses) 528-c

AUTHOR INDEX

A

ADAIR, F. L. *465
 ADAMS, F. D. 265—cr
 ADAMS, R. 560—cr
 ADAMS, R. D. 36—mr
 ALBRIGHT, F. 190—cr
 ALBRIGHT, H. L. *363
 ALEXANDER, E., JR. *374
 ALLEN, A. W. *780
 ALTSCHULE, M. D. *477
 ANDERSON, L. E. *653
 AUB, J. C. 190—cr
 AVERY, B. F. 13—MMS
 AYER, J. B. 844—cr

B

BARNEY, J. D. 521—cr
 BARTLETT, C. J. 337—c
 BAUER, W. *395, *442
 BEASER, S. B. *43
 BECK, I. A. 938—mr
 BECKMAN, W. W. 802—cr
 BELL, C. *901
 BENEDICT, E. B. 1013—MMS
 BEQUAERT, J. C. 856—mr
 BILLIG, O. *253
 BISHOP, W. 311—cr
 BLAND, E. F. 1000, 1047—cr
 BLOOD, R. O. *787
 BLOTNER, H. *287
 BLUMGART, H. L. *874
 BOSWORTH, B. M. *95
 BOTSFORD, T. W. *657
 BOWMAN, R. O. 938—mr
 BOYER, N. H. *628
 BRAILEY, A. G. 645—cr
 BREED, W. B. 22, 677, 881—cr
 BREWSTER, H. H. *822
 BREYFOGLE, H. S. 856—mr
 BROWN, H. W. 811—mr
 BROWN, M. *636
 BROWNE, W. E. 530—mr
 BUDDINGTON, W. T. *400
 BUNNELL, S. 531—mr
 BUTLER, A. M. 485, 802—cr

C

CASS, J. W. 964—cr
 CASTLEMAN, B. 37—mr
 CATTELL, R. B. 494—mr
 CHURCHILL, E. D. 22—cr; 495—mr;
 557, 560, 606—cr
 CHUTE, R. *863
 CLARKE, B. G. *338
 CLUTE, H. M. *363, *508, *701, *727
 COHEN, B. *336
 COLBY, F. H. 311—cr
 COMEAU, W. J. *134
 CONSALES, P. A. *545
 COPE, O. 26—cr; *870
 CORWIN, W. *901
 CUNNINGHAM, A. R. 572—c
 CUTLER, E. C. 7—MMS; 86—mr

D

DALAND, E. M. 194, 352, 451, 961—cr
 DENNY-BROWN, D. 771, 813—MMS
 DENORMANDIE, R. L. *121, *499, *533
 DEROW, H. A. *827
 DIAMOND, L. K. *857
 DIENES, L. 36, 37—mr
 DIEUAIDE, F. R. 267, 603, 642—cr
 DINGLE, J. H. *342, *378
 DITMORE, D. C. *409
 DOCK, W. 201—mr; *633
 DOWNING, J. G. *408; 426—c; *539
 DRESSER, R. *410
 DUSTIN, C. C. *733, *785

E

ELLIS, L. B. 652—c
 ENDERS, J. F. 162—MMS
 ENGEL, F. L. *470
 ENGEL, G. L. *470
 EPSTEIN, L. *357
 EVANS, L. R. *949

F

FAGAN 937—mr
 FAXON, N. W. 493—c
 FINESINGER, J. E. *578
 FINLAND, M. *342, *378; 528—mr
 FISCHER, J. 157—c
 FITZ, R. 2—MMS; *262
 FLAKE, C. G. *1021
 FLYNN, J. E. 529—mr
 FOISIE, P. S. *45
 FOLEY, J. A. 664—MMS
 FRANSEEN, C. 715—cr
 FREEDBERG, A. S. *874
 FREEDMAN, M. A. *370
 FREIS, E. D. *590
 FREMONT-SMITH, M. 922—cr
 FRIEDGOOD, H. B. *788

G

GALLAGHER, C. D. *691
 GALLAGHER, J. R. *691
 GALLAGHER, J. V. 811—c
 GALLUPE, H. Q. 200, 528, 726, 892,
 937—c
 GILMAN, B. B. *400
 GILMAN, S. *102
 GLENDY, R. E. 452—cr
 GOLDSTEIN, A. 769—c
 GOODMAN 937—mr
 GORDON, A. *357
 GRANT, F. C. 109—cr
 GREEN, W. T. 840—cr
 GUILDER, R. P. *619

H

HAC, L. R. *465
 HAMLIN, E., JR. 386—cr; 529—mr

HAMMAN, L. 275—mr
 HAMPTON, A. O. 77, 311, 351, 386—cr
 HARWOOD, R. 681—cr
 HAYES, M. *357
 HAYNES, W. G. *825
 HILL, F. T. *662
 HOFF, H. E. *136
 HOFFMAN, R. *893
 HOLMES, A. D. *909
 HOLMES, G. W. 503—MMS; 557, 560,
 606, 642, 712, 762, 799, 840,
 881—cr
 HURWITZ, A. *46
 HYDE, R. W. *241

I

INGRAHAM, F. D. *374

J

JAKMAUH, P. J. 206—MMS; 571—c
 JANEWAY, C. A. 989, *1029
 JANKELSON, I. R. *548
 JFGHERS, H. *221
 JETTER, W. W. 894—mr
 JONES, C. M. 759—cr
 JONES, T. D. 961—cr
 JOSLIN, E. P. *175

K

KAPNICK, I. *944
 KATZMAN, J. 938—mr
 KAUFMANN, G. G. *691
 KING, D. S. 77—cr
 KIRBY, W. M. M. *730
 KLEMPERER, F. W. 762—cr
 KRANES, A. 1000—cr
 KUBIK, C. S. 36—mr; 109, 844—cr
 KUHN, J. G. *975
 KUNKEL, P. *287

L

LAHEY, F. H. 1—MMS
 LANDESMAN, H. M. 725—c
 LANE, C. G. *39, *293
 LARSON, C. B. 352—cr
 LAWRENCE, K. B. *701, *727
 LEARY, T. 573—mr
 LEE, H. G. 1056—MMS
 LEONARD, C. S. *216
 LERMAN, J. 26, 606—cr
 LINDEMANN, E. *584
 LINENTHAL, H. *433
 LINGLEY, J. R. 1045, 1047—cr
 LINTON, R. R. 229—cr
 LOMAN, J. *439
 LUND, C. C. *247
 LYNCH, D. L. 209—MMS
 LYONS, C. 530—mr; *944

M

MACCOLLUM, D. W. *331; 359—mr
 MACPHERSON, D. J. *575

MAIETTA, A. L. *985
 MAISEL, B 922-cr
 MALLORY, T. B *955
 MARBLE, H 426, 530-mr
 MARCIL, O J *901
 MASSEIL, T B *43
 MAZER, H *174
 McCLOURE, C W. *548
 McKittrick, L. S 351, 386, 388-cr
 MEANS, J H *594, 799-cr
 MELANED, A M *325
 MELENEY, H E 159-MMS
 MENKIN, M F *552
 MERRILL, D 85-c
 MERRITT, H H 358-mr
 MESSINA, S J *408
 MICHELSEN, J 111-cr
 MILLER, E S *949
 MOORE, M *699
 MORAN, R J *988
 MORITZ, A 726, 855, 894-mr
 MOSS, R R *590
 MOTT, F E *174
 MUELLER, W *617
 MULLER, J 572-c
 MUNRO, D *87, *939
 MYERS, R R. *660
 MYERSON, A *336, *403, *439

N

NATERMAN, H L *736
 NATHANSON, I T *830
 NEUSWANGER, C H *626
 NICHOLSON, M J *636
 NICKERSON, D 690-c

O

O'HARA, D 572, 769-c

P

PALMER, R S 156, 425, 689-c
 PASTERNAK, J G *953
 PHIPPEN, W G 810-c
 PITTMAN, H S 230, 557-cr
 PLACE, E H 322-mr
 POLLAK, O J 855-mr
 POPPEL, M H *325
 POWERS, G *612
 PRATHER, G C *169
 PRATT, J H *695
 PRATT, J M 166-MMS
 PRESS, E *475
 PRIEN, E L. *46

PUGH, E A. *624
 PUTNAM, H 322-c

Q

QUINBY, W C 414-cr,
 *512, 521-cr

R

RANTZ, L A *730
 REGGIO, A W 10-MMS
 REIFENSTEIN, C C 145-cr
 RICHARDSON, W 311, 712-cr
 RIVARD, A 937-mr
 ROBBINS, L L 194, 229, 265, 267,
 414, 996-cr
 ROBEY, W H 652-c
 ROCK, J *552
 ROOT, H F *175
 RUDY, A *893
 RUZSCHI, J 922-cr

S

SCHIATZKI, R *18 22, 190, 488, 715,
 885-cr
 SFIRAB, E V *901
 SEWALL, K W *781
 SHORT, C L *390 442*
 SIGLER, L H 725-c
 SILBERT, S 237-mr
 SIMMONS, C C 458, 1011-MMS
 SMITH, G G 314-cr
 SMITH, H W 854-mr
 SMITH, L *210
 SMITH, R M 236-mr
 SMITH, W E 36-mr
 SMITH PETERSEN, M N 143-cr
 SMITHWICK, R H 388-cr
 SOLOMON, P *427
 SOWLES, H K 489-cr
 SPERAGUE, J S *508
 STARR, A *102
 STEWART, J D *480, *944
 STOKES, J 237-mr
 STRIEDER, J W 996-cr
 SULLIVAN, D J *253
 SULLIVAN, E R. 1047-cr
 SWEET, R H 265, 267, 645-cr

T

TALLOV, R H *395
 TAYLOR, G W. 1045-cr

THOMAS, L 358-mr
 THURMON, F M *128
 TOUSANT, E S 274-c
 TROWBRIDGE, L S *699
 TUCKER, C A *1021

U

ULFELDER, H *780
 URMV, T V 75, 418-cr

V

VAN GORDER, G W *737
 VERMONTEN, V *626
 VONDERLEHR, R A 203-MMS
 VON STORCH, T J C *699
 VOSE, S N *277

W

WALKER, W G 120-c
 WASSERSUG, J D *436
 WATKINS, A L *48
 WATSON, C J *665, *705
 WELCH, C E *470
 WELCH, E J *1025
 WELLS, C E 236-c
 WESSFLOHEFT, C *277
 WEYLER, H *733 *785
 WHEATLEY, F E 158-mr
 WHITE P D 77, 516, 603, 927, 961 -
 cr, *980
 WILINSKY, C F 15-MMS
 WILKINS, R W *104
 WILLIAMS, C 516-cr
 WILLIAMS, H W 938-mr
 WILLIAMS, R J 938-mr
 WILLIAMS, W W *905
 WILLIS, W H 769-c
 WILLETTS, A T *863
 WOLFSON, L 573-mr
 WOLFFMAN, O J, Jr *822
 WYMAN, S *703

Y

YOUNG, E L. *703

Z

ZOLLINGER, R M *370, *660
 ZOURABOFF 937-mr

INDEX

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

1942

The date of publication of any case may be determined from the case number. The first two figures of each case number indicate the volume number, 28. The third and fourth figures give the number of the week, dating from January 1. The last figure gives the case number for the week. For example, Case 28421 is the first case for the 42nd week of Volume 28.

- Abscess, of kidney, 28371
 - of liver, 28432
 - of lung, 28271, 28322, 28512
 - retroperitoneal, 28491
 - subdural, 28302
- Adenoma, of parathyroid, 28272, 28311
 - of pituitary, chromophobic type, 28292
- Adrenal, carcinoma of, metastatic, 28271, 28302
 - infarction of, 28292
- Aneurysm, congenital, cerebral, 28151, 28152
 - dissecting, of aorta, with rupture, 28072, 28111, 28202, 28421, 28442, 28451
 - syphilitic, of aorta, 28271
 - with rupture, 28092
- Anomaly, congenital, adhesive band obstructing small bowel, 28062
 - (See also Heart)
- Aorta, hypoplasia of, 28532
 - media necrosis cystica of, 28072, 28442
 - (See also Aneurysm)
- Appendicitis, acute gangrenous, with rupture, 28432
 - healing, 28452
- Appendix, mucocele of, 28051
- Arterioles, hypertrophy of, pulmonary, 28041, 28401
 - with endarteritis, 28041
- Artery, see Aneurysm, Embolism, Heart, Thrombosis
- Bile duct, carcinoma of, 28331
 - stone in, 28121
- Bone, carcinoma of, metastatic, of rib and vertebra, 28191
 - cyst of, humerus, 28312
 - giant cell tumor of, humerus, 28141
 - granuloma of (Hand-Schüller-Christian type), 28101, 28481
 - osteitis fibrosa cystica of, 28311
 - osteoid osteoma of, vertebra, 28291
 - osteomyelitis of, frontal, 28301
 - osteosarcoma of, maxilla, 28142
- Brain, aneurysm, congenital, 28151, 28152
 - carcinoma of, metastatic, 28302
 - embolism of, 28032
 - empyema of, subdural, 28301
 - hemorrhage into, 28151
 - infarct of, 28032, 28482
 - syphilis of, meningovascular, 28332
 - thrombophlebitis, 28301
 - tuberculoma of, 28261
 - tuberculosis of, 28192, 28261
 - (See also Meningitis, Thrombosis)
- Bronchus, cyst of, 28412
 - tuberculosis of, 28201
- Bursitis, tuberculous, 28462
- Carcinoma, of ampulla of Vater, 28331
 - of colon, 28162, 28492
 - of duodenum, 28232
 - of esophagus, 28021, 28322
 - of jejunum, 28181
 - of kidney, 28191, 28342, 28371
 - of liver (hepatoma), 28522
 - of lung, bronchiogenic, 28271, 28282, 28322, 28512
 - of pancreas, 28022, 28031, 28232, 28241, 28471
 - of retroperitoneal nodes, metastatic, from carcinoma of cervix, 28082, 28471
 - of sigmoid, 28172
 - with perforation, 28381
 - of uterus, 28071
- Cholangitis, acute, intrahepatic, 28332
- Choledocholithiasis, intrahepatic, 28121
- Cirrhosis, see Liver
- Colitis, see Intestine
- Cyst of bone, humerus, 28312
 - of kidney, 28342
 - of ovary, 28531
 - bronchiogenic, arising from trachea, 28412
 - echinococcal, 28132, 28461
 - pleuropericardial, 28422
- Degeneration of spinal cord, 28091, 28382
- Diabetes mellitus, 28372
- Diverticulum, see Intestine
- Embolism, of brain, 28032
 - pulmonary, 28022, 28091, 28182
- Emphysema, pulmonary, 28101, 28211
- Empyema, pleural, 28322
 - subdural, 28301
- Endarteritis, pulmonary, 28041
- Endocarditis, see Heart
- Endometriosis, of sigmoid, 28351
 - of uterus, 28351
- Enteritis, see Intestine
- Esophagus, carcinoma of, 28021, 28322
- Fibroma, neuro-, of mediastinum, 28311, 28411
- Fistula, esophagotracheal, 28021
 - ileosigmoidal, 28491
 - jejuno-colic, 28492
- Gall bladder, erosion of, 28332
 - hydrops of, 28241, 28321
- Gangrene of Meckel's diverticulum, 28062
- Hand-Schüller-Christian syndrome, 28101, 28481
- Heart
 - Congenital, interventricular septal defect (cor triloculare) 28532
 - Cor pulmonale, 28041, 28091, 28382, 28401
 - Coronary disease of, thrombosis, 28032, 28182
 - Dilatation of, 28042
 - Endocarditis, bacterial, acute, 28231
 - subacute, mitral, 28341
 - tricuspid (type 6 pneumococcus) 28532
 - calcareous, with stenosis, aortic, 28502
 - rheumatic, chronic, aortic, 28341
 - with stenosis, 28182
 - mitral, with stenosis, 28182, 28341
 - Hypertrophy, hypertensive, 28151
 - idiopathic, 28042, 28102

- Infarction of, 28182
 Pericardium, cyst, pleuropericardial, 28422
 hemo-, 28072, 28111, 28442
 pericardium, uremic, acute, 28012
Thrombus, mural, right auricle, 28042
 Hemorrhage, pulmonary, 28131
 subarachnoid, 26151
 Hemothorax, 26092
 Hodgkins disease, see Lymphoma
 Humerus, cyst of, 28312
 giant-cell tumor of, 28141
 Hypernephroma see Kidney, carcinoma of
 Hyperparathyroidism 28272, 26311
 Ileum, see Intestine
 Infarct, of adrenal, 26292
 of brain, 28032, 28492
 of heart, 28192
 of intestine, 28052, 28362
 of kidney, 28231
 of lung, 28042, 28091, 28182
 of omentum, 28061
 of spinal cord, 28092
 Intestine, carcinoma of, 28162, 28172, 26181, 26232, 28497
 with perforation, 28381
 colic, ulcerative, acute idiopathic with perforation
 28252
 diverticulus of, 28171
 diverticulum of, Meckel's, 28081
 gangrene of, 28062
 inflammation of, 28452
 endometriosis of, 28351
 fistula of, 28491, 26492
 ileitis, regional, 28081
 infarction of, acute, 28092
 venous, 28362
 intussusception of, 26392
 lymphoma of, clasmatic type, 28491
 lymphoblastic type, 26361
 stem cell type, 28242
 obstruction of, 28062
 due to phytobezoar, 28212
 perforation of, (foreign body), 28222
 polyp of, 28392
 tuberculosis of, 28192
 ulcer of, peptic, perforating, 28332
 tuberculous, perforating, 26192
 Kidney, carcinoma of, 28191, 28342
 with abscess, 28371
 cyst of, 28191, 28342
 glomerulosclerosis of, intercapillary, chronic, 28372
 infarct of, 28731
 (See also Nephritis, Nephrolithiasis, Nephrosis)
 Kneec, buritis, tuberculosis of, 28462
 metaplasia, chondromatous, of synovia of, 28127
 Kyphoscoliosis, right dorsal, extreme, 28382
 Liver, abscess of, 28432
 atrophy of, subacute yellow, 28391
 carcinoma of (hepatoma), 28522
 metastatic, 28031, 28471
 cirrhosis of, biliary, 28121
 obstructive, 28101
 portal, 28251
 syphilitic, *hepar lobatum*, 26441
 toxic, 28281, 28522
 cyst of, echinococcal, 28132, 28461
 sarcof of, 28161
 Lung, abscess of, 28271, 28322
 atelectasis of, congenital, 28401
 bronchiectasis of, 28021, 28521
 carcinoma of, 28271, 28282, 28322, 28512
 metastatic, 28031, 28191, 28471
 cyst of, arising from trachea, 28412
 edema of, 28511
 embolism of, 28022, 28091, 28182
 emphysema of, 28101, 28211
 fibrosis of, 28211
 hemorrhage into, 28131
 infarct of, 28041, 28091, 28182
 hypertrophy of, arteriolar, 28041, 28401
 with endarteritis, 28041
 pneumonia of, 28211
 thrombosis of, 28022, 28091
 tuberculosis of, bronchus, 28201
 Lymphoma, malignant, clasmatic type of mesentery,
 28491
 lymphoblastic type, of ileum, 28361
 Hodgkins sarcoma type, of lymph nodes, spleen and
 bone marrow, 28431
 stem-cell type, of ileum and jejunum, 28242
 Maxilla, osteogenic sarcoma of, 28142
 Medrinum, adenoma of, parathyroid, 28272
 fibroma of, neuro-, 28311, 28411
 Meninges, carcinoma of, metastatic, 28302
 syphilis of, 28332
 tuberculosis of, 28192 28261
 Mucocoele, of appendix, 28051
 Nephritis, glomerulo-, acute, 28131, 28211, 28331, 28262
 chronic, 28012, 28262
 subacute, 28112 28341
 Nephrolithiasis (sulfadiazine), 28271
 Nephrosis, lipid 28472
 sulfonamide, 28501
 Omentum, cyst of, echinococcal (gastrocolic) 28461
 infarction of, 28061
 Osteitis, fibrosa cystica, 28311
 Osteoma, osteoid, of vertebra, 28291
 Osteomyelitis frontal, 28301
 Ovary, pseudomucinous cyst of, 28531
 Pancreas, carcinoma of, 28022, 28031, 28232, 28241 26471
 fibrosis of (chylia), 28252
 Pancreatitis, acute, hemorrhagic, 28221, 28511
 chronic, with fat necrosis, 28121 28502
 Parathyroid, adenoma of, 28272, 28311
 hyperplasia of, 28272
 Pericardium, see Heart
 Peritoneum, carcinoma of, metastatic, 28471
 Peritonitis, acute, 26221, 28252, 28332
 bile, 28121
 Cl welchii, 28222
 streptococcal, 28472
 tuberculous, encapsulated, with calcification 28531
 Pituitary, adenoma of, 26792
 Pleura, carcinoma of metastatic 28031
 empyema of, 28322
 Polyp of ileum, 28392
 Pylephlebitis, suppurative, 28432
 Rectum, see Intestine
 Rib, carcinoma of, metastatic, 28191
 Sarcoid, of liver, 28161
 Sarcoma, Hodgkins, see Lymphoma
 lipos, of thigh, 28052
 lympho-, see Lymphoma
 osteogenic, of maxilla, 28142
 Sigmoid, see Intestine
 Sinus, thrombophlebitis of, longitudinal, 28301
 Sinusitis frontal, 28301
 Spinal cord, degeneration of 28091, 28382
 infarction of, 28092
 Spleen, lymphoma of, 28431
 Splenomegaly, 28251 28281

Stomach, carcinoma of, 28302
 metastatic, 28471
 Sulfonamide therapy, 28271, 28501
 Synovia, chondromatous metaplasia of, 28122
 Synovioma, of thigh, 28352
 Syphilis, of aorta, with aneurysm, 28271
 rupture of, 28092
 of liver, 28441
 meningovascular, 28332
 Thigh, sarcoma of, lipo-, 28052
 synovioma of, 28352
 Thrombophlebitis, of superior longitudinal sinus, 28301
 Thrombosis, of basilar artery, 28482
 of mesenteric vein, 28082, 28362
 of portal vein, 28082, 28362
 of pulmonary artery, 28022, 28091
 of renal vein, 28471
 of splenic vein, 28082, 28222, 28362, 28471
 (Sec also Heart, coronary disease of)
 Trachea, cyst of, bronchiogenic, 28412
 Tuberculoma, of brain, 28261
 Tuberculosis, of bronchus, 28201
 of duodenum, with perforation, 28192
 of knee, 28462
 of meninges, 28192, 28261
 of peritoneum, 28011, 28531
 miliary, 28011, 28192
 Ulcer, of duodenum, chronic, with perforation, 28332
 Urolithiasis medicamentosa (sulfadiazine), 28271
 Uterus, endometriosis of, 28351
 carcinoma of, 28071, 28082
 Vein, pylephlebitis of, 28432
 thrombosis of, 28082, 28222, 28362, 28471
 Vena cava, obstruction of, by hepatoma, 28522
 Vertebra, carcinoma of, metastatic, 28191, 28322
 ostcoma of, osteoid, 28291

SPEAKERS IN DISCUSSIONS OR AUTHORS OTHER THAN DR. TRACY B. MALLORY

Adams, F. Dennette, 28011, 28331
 Adams, Ralph, 28412
 Allen, Arthur W., 28121, 28212, 28221
 Aub, Joseph C. 28311
 Ayer, James B., 28151
 Baker, Myles B., 28192
 Barney, J. Dellinger, 28402
 Bartlett, Marshall K., 28071
 Beckman, William W., 28472
 Benedict, Edward B., 28011, 28132, 28161, 28201
 Bishop, William, 28341
 Bland, Edward F., 28041, 28202, 28522, 28532
 Brailey, Allen G., 28162, 28432
 Breed, William B., 28111, 28271, 28441, 28491
 Burbank, Charles, 28531
 Butler, Allan M., 28211, 28252, 28262, 28391, 28472
 Cass, John W., 28512
 Castleman, Benjamin, 28012, 28032
 Churchill, Edward D., 28201, 28271, 28411, 28412, 28422
 Colby, Fletcher H., 28231, 28341, 28491
 Cope, Oliver, 28272, 28311
 Daland, Ernest M., 28312, 28352, 28381, 28511
 Davenport, Lowrey F., 28021, 28191
 Dicuaide, Francis R., 28012, 28092, 28251, 28332, 28421, 28431
 Dock, William, 28031
 Farber, Sidney, 28101, 28252, 28262
 Faxon, Henry H., 28172
 Fitzhugh, Greene, 28231
 Franseen, C. C., 28452
 Fremont-Smith, Maurice, 28111, 28151, 28501

Garland, Joseph, 28252
 Gens, John P., 28342
 Glendy, Robert E., 28182, 28382
 Graham, John R., 28232
 Grant, Francis C., 28301
 Graybiel, Ashton, 28012, 28042
 Green, William T., 28481
 Hamlin, Edward, Jr., 28061, 28091, 28121, 28361
 Hampton, Aubrey O., 28101, 28161, 28162, 28171, 28191, 28192, 28201, 28231, 28261, 28341, 28351, 28361
 Harwood, Rced, 28442
 Hayden, E. Parker, 28242
 Holmes, George W., 28031, 28122, 28181, 28232, 28411, 28412, 28422, 28431, 28451, 28461, 28462, 28471, 28481, 28491
 Jeffries, William M., 28131
 Jones, Chester, 28162, 28232, 28461
 Jones, T. Duckett, 28041, 28511
 King, Donald, 28201, 28282, 28091
 Klemperer, Fridrich W., 28462
 Kranes, Alfred, 28061, 28131, 28522
 Kubik, Charles S., 28091, 28151, 28152, 28261, 28301, 28482
 Larson, Carroll B., 28351
 Lerman, Jacob, 28272, 28422, 28502
 Lingley, James R., 28011, 28042, 28051, 28061, 28531, 28532
 Linton, Robert R., 28181, 28321
 Lowis, Samuel, 28261
 Ludwig, Alfred O., 28072
 Lyons, Champ, 28211, 28222, 28231
 Maisel, Bernard, 28501
 McKittrick, Leland S., 28051, 28061, 28132, 28351, 28361, 28362
 Means, James H., 28091, 28112, 28471
 Michelsen, Jost, 28302
 Mueller, Harry L., 28101
 Parsons, Langdon, 28082
 Penfield, Wilder, 28261
 Pittman, Helen S., 28322, 28411
 Quinby, William C., 28371, 28402
 Reifenstein, Edward C., Jr., 28292
 Richardson, Wyman, 28081, 28112, 28162, 28241, 28341, 28451
 Robbins, Laurence L., 28312, 28321, 28332, 28341, 28352, 28521
 Ropes, Marian W., 28231
 Ruesch, Jurgen, 28501
 Sarris, S. Peter, 28062, 28122
 Schatzki, Richard, 28021, 28252, 28271, 28311, 28392, 28452, 28492
 Simmons, Channing C., 28141
 Smith, George G., 28342, 28501
 Smith, William D., 28202
 Smith-Petersen, Marius N., 28291
 Smithwick, Reginald M., 28212, 28362
 Sowles, Horace K., 28392
 Strieder, John W., 28521
 Sullivan, Eugene R., 28531
 Sweet, Richard H., 28221, 28332, 28432
 Talbott, John H., 28022, 28211, 28251, 28531
 Taylor, Grantley W., 28531
 Tobey, Harold G., 28142
 Ulfelder, Howard, 28132
 Urmy, Thomas V., 28081, 28281, 28372
 Van Gorder, George W., 28141
 Wallace, Richard H., 28052
 Welch, Claude E., 28061, 28122, 28162, 28171
 White, Paul D., 28012, 28032, 28042, 28102, 28202, 28282, 28401, 28421, 28502, 28511
 Williams, Conger, 28401
 Young, Edward L., 28171
 Zeller, Wallace, 28251

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NUMBER I

THE RELATION OF MEDICINE TO THE EMERGENCY*

FRANK H. LAHEY, M.D.†

BOSTON

CERTAINLY, after what we have been through in this country and what we have seen other countries go through, no one can fail to say that we have been slow to convince, slow to profit by such tragic examples in other countries, slow to suspect and slow to prepare, and that we have likewise been woefully slow in accelerating our war effort. No one can truly say that many of our leaders have not been aware of the fogginess concerning this situation, or that these leaders have not warned us of our dangers. As a moral example to ourselves as we face our truly dangerous future, we must admit that we have stupidly believed what we wanted to believe, in the face of the fact that to anyone with simple, unbiased sense it was evident that the true situation was what we did not like it to be. Experience is often bitter medicine to take, but even though we seem stupid to ourselves as we review the past year, we should have much to be thankful for if we were even now to learn the lesson that the situation the country finds itself in is not what we should like it to be, and that to make it so will require our every resource in energy, unity, courage, speed and tenacity.

One of the things that has impressed me as I have traveled the country urging on the medical profession the need for physicians is that the country is so sensitized to rumors. If we could only realize that rumors, innuendoes and gossip are such bad things! Whoever heard of a good rumor? A rumor is always bad. If we could but realize that rumors, innuendoes and gossip tend to lend aid to our enemies by promoting confusion, discord and strife, we should, I am sure, avoid the spread of such rumors. I have endeavored to develop for myself a philosophy for this emergency, and it is that in place of rumors I shall employ, when I am so inclined, frank criticism. It has at least the virtue of honesty of purpose, and of willingness to accept the penalties that go with

responsibility if I am wrong. Criticisms of our neighbors and their war efforts — and in times such as these they become prevalent — are often an apology for our own shortcomings or an attempt to publicize and make prominent whatever we have done by attracting attention to it by comparison with others. Conscientious labor and true patriotism are practiced for the convictions that go with them. Their consistent performance brings to the possessors of these convictions all the reward they require. Publicizing of the virtue of patriotism questions not only the pureness of its quality but also, as publicized charity does, the sincerity of its purpose.

Every doctor, I am certain, is particularly interested in what the immediate needs for the services are, and since I am in regular contact with the offices of the Surgeons General in Washington through the Procurement and Assignment Service, it is possible for me to state quite accurately what these needs are. To meet the requirements of its rapidly mounting numbers, the Army must have twelve thousand additional doctors by January 1. To meet the immediate needs of aviation and the Army, it must have seven thousand doctors by July 1. These are not probable needs; they are real needs if we are to maintain the table levels that are now accepted for the Army — 6.5 physicians per 1000 men, 15 dentists, and 0.75 veterinarians.

The immediate need for doctors to go with troops is in the age group up to thirty seven, and for specialists in that up to forty five. Why is it necessary for the Army to have age groups such as these? The reason should be obvious to everyone: this is a war of many and distant fronts. We are all conscious of the fact that cargo space is at a premium, and to ship a doctor of greater age than this is to accept the possibility of his breakdown in a distant place; such an event would require not only more cargo space to get someone there to take his place but also the services of those who have already been transported there to take care of

*An address delivered at the annual banquet of the Massachusetts Medical Society, Boston, May 26, 1942.
†President, American Medical Association.

him and feed him. This is a bald and plain statement why age groups such as these are desirable.

Older men have frequently asked me whether there would be an opportunity for them in this war. There will undoubtedly be an opportunity for everyone if the war goes on long enough, as it very well may. The demand for doctors will be so great that everyone from all the various age groups will be required either in industry and hospitals, to care for the civilian population, or in other branches of the national endeavor. We must all realize in civilian life that there will be not only adjustments, such as those to sugar and to tires and gasoline rationing, but also, as the situation becomes more acute and the endeavor more prolonged, changes and modifications in medical care; the civilian population must adjust its mind as satisfactorily to these rationings as to the more tangible and obvious ones, such as things to eat, to wear or to ride in.

Finally, I should like to urge the profession in general, particularly physicians under forty-five, who fall under selective-service regulations, to volunteer at once and not wait further. The need for medical personnel, particularly for aviation and the Army, is so urgent that if they are not already

listed by their state chairman of the Procurement and Assignment Service as essential for a medical school, hospital, civilian population or industry, they should by all means immediately seek a commission. Every doctor of forty-five or under must realize that he is actually in the hands of the Selective Service System and that he is being deferred in Class 2-A only up to the time when it is determined that he is either essential—this decision being made by the state committee of the Procurement and Assignment Service—or not essential. Whenever he has been listed as not essential, he becomes literally and actually subject to induction.

It is with no purpose of threat that I make these statements. The Army must have medical personnel. It has deferred by presidential request to the Procurement and Assignment Service until such time as essentialness has been settled, and should it not obtain the necessary number of doctors by voluntary enlistment, there is no way to obtain them except by requesting selective-service boards to change the status of these men from deferred classification in Class 2-A to draftability in Class 1-A. It is to be hoped that compulsion in this emergency will not be necessary.

605 Commonwealth Avenue

THE PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS IN MASSACHUSETTS*

REGINALD FITZ, M.D.†

BOSTON

THE Procurement and Assignment Service for Physicians, Dentists and Veterinarians, established recently in the office of Defense, Health and Welfare Services, is an interesting experiment in medical democracy. So far as doctors are concerned, it is designed to give every qualified physician an opportunity to enroll himself in one of the several services demanded by the national need. An enrollment form and a questionnaire have been circulated recently, which all physicians should fill out carefully and at once. Only with the information that will be obtained from these forms can the Procurement and Assignment Service perform its functions intelligently and expeditiously.

The Procurement and Assignment Service for Physicians began to function in Massachusetts on

January 30, 1942. The method by which this service might operate most effectively has necessitated the establishment of a central corps-area committee for New England under the chairmanship of Dr. Walter G. Phippen; under him are appropriate state and district subcommittees whose duties are to obtain as many doctors as possible for military use and at the same time to see to it that the civilian needs of medical care in each community are unhampered. This report of the first three months' experience is now presented by the Massachusetts committee.

The Army, Navy and Public Health Service wish to attract officers as volunteers, not by induction; thus, each person who applies for a commission through the Procurement and Assignment Service does so voluntarily. To be eligible for a commission in any of the national services, a man must be a citizen of the United States and a graduate from a medical school acceptable to the medical departments of the United States Army or Navy or to other federal agencies. He must have

*Presented at the annual meeting of the Massachusetts Medical Society, May 27, 1942, and as a report to the Council of the Massachusetts Medical Society from the Massachusetts Committee of Procurement and Assignment Service. The members of this committee are: H. M. Clute, J. J. Curley, E. L. Kickham, Dwight O'Hara, W. H. Pulsifer and Reginald Fitz, chairman.

†State director for Massachusetts, Procurement and Assignment Service for Physicians

had a twelve-month internship or its equivalent. He must be a licensed practitioner of medicine.

Experience has demonstrated that young physicians make more effective medical officers than older men. The present Army and Navy needs are for physicians under thirty-six years of age. Those under thirty-six desiring immediate commissions may now write to the Procurement and Assignment Service, 601 Pennsylvania Avenue, N. W., Washington, D. C., or may interview Lieutenant Colonel Alexander Marble at 319 Longwood Avenue, Boston. Those who are qualified will receive proper application forms for commissions in the Army or the Navy. The filling out of the enrollment form does not constitute an application for a commission; the man who wishes to volunteer must, in fact, apply to the proper authorities.

One of the first problems presented to the Massachusetts committee has been to analyze the physician complement of Massachusetts in younger men, to determine those who might best be spared for national service by their civilian communities.

In the State, at present, in round numbers, there are 8000 doctors. Of these, approximately 3300 are less than forty-two years old. Women and foreigners are not eligible for commissions. There are a certain number of young men, too, with physical handicaps so serious that even most liberal standards cannot pass them. Their bearers are hopelessly unfitted to withstand the vicissitudes of Army or Navy life. The exact number of women doctors, foreigners and physically unfit men has not been counted accurately, but it is a fair assumption that about 10 per cent of all young doctors will be disqualified from any form of military service for one or the other of these reasons.

Of the 2970 remaining, a certain number will be absorbed in the necessary work of medical teaching. Obviously, if the practice of medicine is to continue, an uninterrupted procession of students must march through the medical schools, and their pathway of effective medical education must be interfered with as little as possible.

Boston University, Harvard University and Tufts College were asked to submit to the Massachusetts committee a list of their medical faculties, marking each member as an "essential" or "available" teacher. When the first lists were completed, the three deans conferred with the state chairman and agreed to revise their lists for the purpose of retaining as "essential" teachers only those under forty-two who in fact were necessary to a smoothly continuing process of medical education. These three faculties employ, ordinarily, 707 such young teachers. Of this large list, only 148 have been retained as "essential." These essential young men are, in the main, engaged in

teaching the preclinical sciences or in working on research essential to national defense. The medical schools have adopted the policy that good clinical teaching can be conducted very largely by older men. Each school has determined to be understaffed rather than overstaffed with young clinical teachers, and thereby has set a good example for unselfish, patriotic conduct to the rest of the country.

Before the Procurement and Assignment Service had become activated, a certain number of men had already volunteered and had been commissioned; others were in the Medical Reserve Corps or National Guard and were called to active duty. The exact number of such medical officers in Massachusetts has not been ascertained, but from known figures it is estimated that at present at least 300 young physicians already are with the armed forces or are commissioned to go on active duty when called.

The various hospitals that train interns and resident physicians or surgeons have presented an interesting problem. Those approved by the American Medical Association for this purpose were written to and were asked to estimate the minimum number of interns and residents with which they could operate effectively each year. There are two types of hospitals in this group, the state institutions and those privately endowed. The state institutions will require a resident staff of about 100 young physicians and, without much question, will obtain them. The privately endowed institutions, on the other hand, claim to need a staff of 490 interns each year and 180 resident and assistant resident physicians or surgeons.

These figures are of considerable interest. The supply of interns is maintained in large measure by recent graduates of medical schools. The accelerated program of medical education adopted by most of the schools in which classes graduate at nine-month intervals instead of annually will do something to maintain the supply. On the other hand, even under the accelerated program, there are not enough students in the Massachusetts schools to yield more than 350 interns a year. Normally, the necessary extras have come from other than local medical schools or from persons who have accepted repeated internship appointments.

After July 1, nearly all medical students will be commissioned officers in the Army or Navy on graduation, likely to be called to active duty on completion of a year's internship. The chance for a man to experience more than a year's internship will be slight. The entire country offers more internships than can be filled so that the supply of men outside Massachusetts coming to our hospitals will be curtailed. And finally, because of the need for medical officers and the large number

of internships available, it is a reasonable assumption that the Surgeons General will permit students but little free time after graduation in which to begin their hospital appointments. All this means that Massachusetts hospitals face a shortage of interns. Hospitals will be fortunate if they can fill, successfully, two thirds of the appointments that they offer. It appears desirable to suggest to the hospitals approved for intern training that they offer twelve-month appointments, to begin as promptly after the end of each medical school academic year as possible, and to warn them of the possibility of being unable to fill all the appointments offered.

The resident situation is even more precarious. An appreciable number of resident physicians and surgeons have already left hospital posts. The armed forces have argued that any healthy doctor with hospital experience of a year's duration is suitable for military service. Many residents, imbued with a high spirit of patriotism, resigned their posts as quickly as possible after Pearl Harbor.

So long as the present emergency lasts, it is reasonable to assume that it will be hard for hospitals to acquire and hold resident physicians and surgeons. They must be drawn largely from those men who are disqualified physically from more active work or from women. The Massachusetts committee, acting on advice from the Surgeons General, is no longer disposed to regard all residents as "essential" men. A few residents occupying responsible posts in large teaching hospitals may be retained.

There are approximately 200 hospitals in Massachusetts. As has been stated, one of the purposes of the Procurement and Assignment Service is to see to it that the civilian needs for medical care in each community are unhampered. Each hospital has been invited to submit to the committee a list of its staff, each member thereon being classified as "available" or "essential." Up to the present time, returns have been received from nearly two thirds of the hospitals in the State. The figures so assembled from the samples given offer suggestive data.

Of 1187 doctors under forty-two years of age who are above the rank of residents on hospital staffs, 512 (43 per cent) are regarded as "essential" to hospital work; 525 (44 per cent) are "available"; and 150 (13 per cent) are already commissioned or have applied for commissions in the Army or Navy.

These figures enable one to visualize, with reasonable accuracy, the present situation in Massachusetts regarding the procurement and assignment of physicians, which is graphically illustrated in Figure 1. If these figures are even as ap-

proximately correct as they are believed to be, a continuous supply of about 1200 young doctors is necessary to the health and welfare of the citizens of Massachusetts, and there is a pool of about 1800 in which must be determined the ones who can be properly claimed as "essential" in their ci-

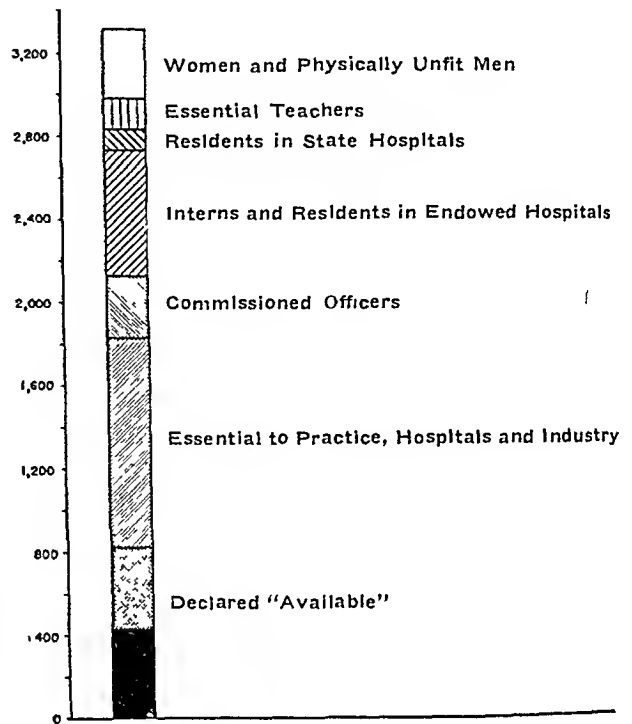


FIGURE 1. *Classification of Physicians in Massachusetts Less than Forty-Two Years of Age.*

vilian capacities, and those to be regarded as "available" for military service.

It is to be emphasized that the medical corps of our armed services are comprised of volunteers and not of inducted men.

Up to the present, the names of those who have volunteered since the Procurement and Assignment Service was established have been forwarded from the central office in Washington or from the corps-area chairman to the state chairman, and he, in turn, has forwarded them to the appropriate district committees. The district committees have studied the case of each name submitted to them and have cleared the owner as "available" or "essential." Finally, the state chairman has made certain, before rendering to Washington his final report, that the person under consideration was not an "essential" teacher or hospital-staff member.

This general policy appears sound and seems to give appropriate consideration to each case. To date, 394 names have been cleared in this manner. Of these, 308 (78 per cent) have been deemed "available" for national service.

This plan of managing the medical profession during the present war is still in the experimental stage. Four hundred "clearances," however, seem a reasonable sample from which to take a preliminary account of stock. For this purpose, a population map of Massachusetts* has been constructed in which each county has been arranged in size according to its population (Fig. 2). In each

tors therein declared "available" (Fig. 3). There appears to be remarkable uniformity in the manner in which local committees operate. So far, no single county has been depleted of its young medical men, and the desire to supply medical officers has not outweighed the need to maintain proper oversight of civilian health.

One interesting impression has developed from

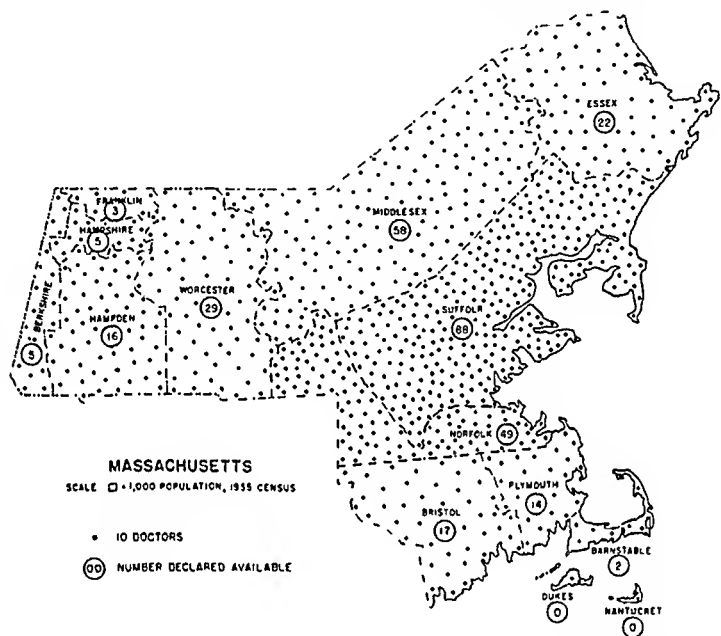


FIGURE 2. Population Map of Massachusetts Showing the Distribution of All Physicians and That of Those Declared "Available" by the Procurement and Assignment Service.

county, the total number of doctors has been listed, each dot on the map representing 10 doctors; and finally, in each county the number so far declared "available" by the Procurement and Assignment Service has been set down.

As can be seen, the distribution of doctors throughout the State is relatively uniform, except that Norfolk and Suffolk counties appear somewhat overcrowded medically. Certainly, the total supply of doctors seems ample for some time to come.

That the local committees have worked honestly in analyzing the list of names sent to them is suggested by a tabulation of the medical population of each county and by the number of doc-

this short experience with the Procurement and Assignment Service. The men whose names have been cleared have come from five sources. They have come from Boston University, Harvard University, Tufts College, approved medical schools from outside Massachusetts, and finally, from schools at present not recognized by the Surgeons General, the most important Massachusetts medical school in this category being Middlesex University. Information has been obtained concerning the number of graduates, from these Massachusetts schools, under forty-two years of age and licensed to practice in Massachusetts. These figures have been compared with the number of men from these schools so far cleared by the Massachusetts committee of the Procurement and Assignment Service. The information obtained in this manner

*This map was constructed by Dr. W. L. Aycock, of the Harvard Medical School. The figures for physicians were taken from the 1940 edition of the American Medical Directory.

and illustrated in Figure 4 is of some interest.

The data suggest very pointedly that young physicians from all medical schools are, at present, willing but are in no great haste to offer their services to the country. On the other hand, there

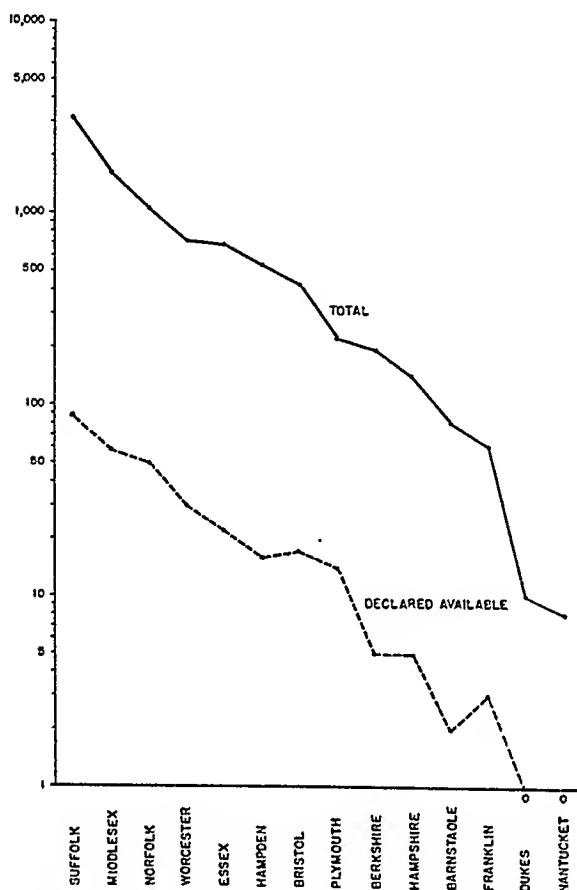


FIGURE 3. *The Relation of "Available" and Total Physicians in the Different Counties of Massachusetts.*

is no desire among any single group to behave selfishly in times like these. The figures offer additional support to the belief that there are large numbers of young physicians in Massachusetts still potentially available for military service.

To certain persons, one annoying aspect of the method of procedure up to date has been the delay between the date of volunteering, of "clearance" by the Procurement and Assignment Service, and of receipt of commission. To offset this, in Massachusetts, a team under the leadership of Lieutenant Colonel Alexander Marble has been established by the Army with power to commission, immediately, men cleared as "available" by the Procurement and Assignment Service. This means that henceforth the commissioning of our medical officers will be greatly accelerated and that annoying delays will be eliminated.

This, in brief, has been the experience of the Procurement and Assignment Service for Physicians in Massachusetts during the first three

months of its existence. On the whole, the method adopted for enrolling medical men in national service seems workable, fair and considerate. The results are already promising and point to the fundamental value of a democratic way of building up a large volunteer medical corps.

When one looks to the future, it is obvious that there are many young doctors in Massachusetts who should enter military service as quickly as possible. Young physicians, especially those in Suffolk and Norfolk counties, where the medical population is so dense, should be enrolled in large numbers. On the other hand, all local committees must continue to see that no region or town in the State is depleted of its young men in the desire to supply medical officers. Civilian needs must not be forgotten.

Most of these young men already declared "available" by their hospitals may well be expected to take up the cudgels of war at once. "Essential" young men will soon be declared "available" to

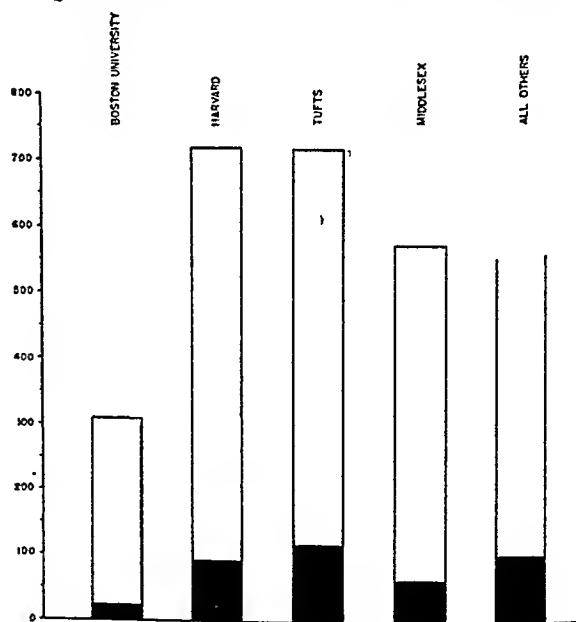


FIGURE 4. *The Source of Young Physicians in Massachusetts.*

The columns represent the numbers of graduates from 1926 to 1941 who are practicing in Massachusetts, the solid portions showing the numbers of those already investigated by the Procurement and Assignment Service. The total number of graduates from medical schools outside Massachusetts is not known.

volunteer, if need be, and as hospitals become adjusted to the view that older men on their staffs are still capable of doing more than a full day's work. The health of the Commonwealth need not suffer from this plan, for there are more than enough doctors to go round. All physicians of Massachusetts will contribute more than their share in doing the work that must be done.

CIVILIAN MEDICAL DEFENSE IN MASSACHUSETTS*

ELLIOTT C CUTLER, MD†

BOSTON

THE Committee on Public Safety welcomes this opportunity to thank the physicians of Massachusetts for their fine co operation and their loyal and generous assistance in organizing for the care of the civilian population injured by enemy action. Up to the time of Pearl Harbor, there were two almost equally divided opinions concerning the necessity for this effort. In fact, the group who thought such efforts were silly and wasteful were the more vociferous. The injuries sustained by civilians in Hawaii and Tokyo had a salutary effect in behalf of those who, although they may not expect bombing, believe that the best defense against it is suitable preparation. One should remember that it has repeatedly been stated in England that gas was not used there because England was better prepared for this dilemma than Germany. Preparation is the best defense.

We here do not need to have an elaborate organization or spend the public funds in setting aside great numbers of empty beds. Sir Wilson Jameson,‡ chief medical officer of the British Ministry of Health, said last winter while he was here, "The tremendous anticipated casualties never did materialize, and it was found that to try to run a service of this kind on a full time basis was not satisfactory." What we need is a simple and mobile organization of our entire facilities. Moreover, in considering any organization, we must conserve trained professional personnel and use, preferably, persons over forty-five years of age or those with physical disabilities that prevent active service with the armed forces.

Civilian medical defense in Massachusetts began with the establishment of the Committee on Public Safety in September, 1940. It was the hope of the Medical Division that a system could be set up that was mobile so that assistance could be obtained from many communities and sent to a distant community if the need proved great enough. It was further hoped that expenditure of public funds could be kept down by avoidance of the permanent dispensary construction that was undertaken in London, and that a minimum of professional personnel could be utilized.

The State Central Committee is composed of the Medical Executive Committee and various sub-

committees, all of which comprise representatives covering the Massachusetts Department of Public Health, the hospitals, the dentists, the nursing organizations, the American Red Cross, the medical examiners of the Commonwealth and the pharmacists. Indeed, all interests that might give aid should disaster occur have their share in this setup. Specialists in gas decontamination and persons who aid in the proper relation of the Medical Division to the Protection Division and Evacuation Division sit on this central board.

The function of the Central Committee was to set up a system that could be utilized throughout the Commonwealth in small rural areas as well as in the large urban centers and to assist the local communities in obtaining the necessary equipment for the task. To assist the committee, there are, in each of the nine regions into which the State has been divided, regional medical heads, who have a group of deputies to help them. These deputies represent more intimately the members of the district societies of the Massachusetts Medical Society, the dentists and the hospital superintendents. They assist directly in stimulating the 351 communities to complete their organizations and give them practice. They help in the distribution of supplies and in the proper blacking out and organization of hospitals. In each of the district warning centers, which are the nerve centers of the information system, a deputy medical head must be at hand to give the controller expert information on medical matters. Information concerning the number of ambulances, first-aid posts and vacant hospital beds in that area must be available. Should these be used up, the deputy medical head must know where others can be obtained. In fact, these regional setups should be so complete that, if the state office at 18 Tremont Street, Boston, were wiped out, relief to the citizens would go on in a competent and satisfactory manner.

The plan now in use in the 351 communities of the Commonwealth puts full authority and responsibility for the setting up of medical assistance on the shoulders of the local chief medical officer. The plan is as follows: in each community, there are four parts to the medical services—first aid parties, mobile medical first-aid posts, transportation facilities and hospitals (Fig. 1).

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 26, 1942.

†Moseley Professor of Surgery, Harvard Medical School, surgeon in chief, Peter Bent Brigham Hospital, director, Medical Division, Massachusetts Committee on Public Safety.

‡Jameson, Sir Wilson. *Hospitals in England Today*. 14 pp. New York: Hospital Council of Greater New York, 1941.

A *first-aid party* consists of six lay people trained in first aid who carry on their persons suitable first-aid equipment. They are sent out to the scene of an incident, where they apply temporary dressings and first aid, guide the walking wounded and carry the stretcher cases to the physicians and nurses in the medical first-aid posts.

A *mobile medical first-aid post* is a group of physicians, nurses and lay people trained in first aid who set up in a building an incident dressing station. There are two doctors and two nurses so that one professional group can take charge of the stretcher cases, and the other group the walking wounded. No attempt should be made to carry out surgery at this point other than the ligation of a bleeding vessel or the control of some dire catastrophe. At such posts, hot drinks should be served by mobile canteens, suitable dressings should be added to the dressings already applied, splints should be readjusted or applied, and morphine should be administered for comfort. The stay in a first-aid post should be minimum, since the critical point in the recovery of injured people is proper surgical care in a hospital.

Transportation facilities. After preliminary dressings and the splinting of fractures have been carried out in the first-aid post, the injured people are taken by some kind of vehicle (and anything that moves on wheels from a sand truck to a beach wagon or a sedan will do) to the nearest emergency hospital.

Hospitals. At the hospital, provisions must be made for one-way traffic. The walking wounded and stretcher cases should be separated and looked after by separate teams. The hospitals must be properly blacked out—at least the admitting rooms, the x-ray departments and the operating rooms. They should be prepared, from now on, to send home convalescent people and noncritically ill medical patients, to make room for casualties, and the hospital staffs must be organized into eight-hour or twelve-hour shifts so that the professional care may go on continuously. We have listed 95 hospitals that have more than 50 beds and are not special hospitals as places suitable for such work, but in a grave emergency, any hospital must be ready to function for this purpose.

In the event of continued bombing, casualty cases and others will be evacuated from metropolitan areas to rural hospitals in the country that have been called "*base hospitals*." At present, some 6000 beds are available in rural state institutions for this purpose. The staffs of these base hospitals will need to be supplemented, and the Medical Division has been given the privilege of nominating certain physicians, preferably over the age of forty-five, for reserve commissions in the United States Public Health Service. It is expected that such reserve officers, when called to active duty, will be ready to leave their homes and practice, put on uniforms and go to service as directed.

The medical equipment and the stretchers, blankets and splints for the desired number of first-aid parties and medical first-aid posts are now being distributed on the basis of two parties and one post per 10,000 inhabitants. Massachusetts, at this ratio of distribution, will require 438 posts. However, since small communities cannot be divided at that ratio, we shall probably end up with about 1000 first-aid posts. The gauze equipment for all these posts has already been provided by the Boston Metropolitan Chapter of the American Red Cross, sterilized at the Peter Bent Brig-

ham Hospital, and delivered to the communities. The pharmaceutical supplies, including morphine, alcohol and other drugs, have been donated by the Massachusetts Pharmaceutical Association and have been distributed to the communities.

Lest anyone should think getting material ready for civilian defense is a little job, imagine the task of dividing 140 pounds of sulfanilamide into 23,000 3-gram lots! In addition to our own labors, we have assembled 65,000 air-raid warden's belts, with their equipment, for the Protection Division. The belt material for the first-aid parties was given by the New England Rainwear Manufacturing Company, and the material was stitched into belts by the Ladies Garment Workers Union, who gave 18,000 hours of free labor. We hope, eventually, to acquire additional medical supplies, splints, stretchers, blankets and so forth from the federal government in Washington, but thus far, all supplies and equipment and training have been arranged locally by the Medical Division of the Committee on Public Safety. (It may seem peculiar to some of you that the federal government has not taken a greater interest in the protection and care of injured citizens, since war is obviously a general governmental undertaking, but all of us must recognize the serious demands on the Government at this time. Criticism will not help, and until each citizen is devoting a part of his time daily to the national welfare, he can scarcely criticize others. Remember that this civilian defense is a voluntary effort and, therefore, perhaps somewhat protected from the chronic "grouser.") Many generous citizens have given time and funds, and an attempt has been made to keep the expenditure of tax funds as low as possible. An especially welcome gift was the receipt of twelve complete field sets (consisting of two boxes of bandages, splints, instruments and drugs) suitable for equipping a medical first-aid post from the Medical and Surgical Relief Committee of America, which has its headquarters in New York City. These sets have been distributed either to vulnerable areas, to areas that deserve assistance because of their generous labors, a reward for virtue or to areas where the expense of equipping such necessary units was beyond local means. Furthermore, through the efforts of the Massachusetts Pharmaceutical Association, 978 emergency medical depots, have been established throughout the state.

The functioning of first-aid parties and posts is similar for all communities (Fig. 1). Information of damage will reach the chief air-raid warden of every report center in that area. The chief medical officer will then send to the incident the proper number of first-aid parties and posts in vehicles, later to be used to transport the wounded. From the first-aid posts, the injured will go to

the nearest hospital, whence, after an interchange of blankets and splints, the ambulances will return to the first-aid posts.

The Medical Division has further responsibilities such as the care of persons who are gassed. In this responsibility are two groups. The first includes those simply gassed but uninjured. Such persons will be taken to a gas decontamination center, where they will be denuded of their cloth-

simple gas decontamination annex, which must have at least two rooms separated by a gas lock. There must be one area in which to rid a gassed person of contaminated clothing and another area in which to decontaminate the victim by washing before he is admitted to the hospital for further surgical care.

A particularly happy phase of the work concerns our relations with the United States Public Health Service. Through their generosity, two members of the Medical Division will hold commissions in that federal branch. We are further authorized, as previously stated, to set up reserve affiliated units in the Public Health Service. In addition, we can utilize certain of our colleagues as consultants in the United States Public Health Service should the magnitude of the occasion necessitate such service. Another activity has been the gift to the Commonwealth of large funds to be invested in the establishment of blood banks. These will serve not only for the military period but also as a permanent contribution to better medical care in this state. Finally, through this same source, the cost of the care of civilians injured by enemy action will be borne by the federal government, including those injured by sabotage, in blackouts and from direct enemy action by combat forces.

Another essential relation is that to the Evacuation Division. In the coastal areas, this division's activities may be of the greatest moment, either because of enemy action or because the military commanders order the evacuation of seacoast districts. The movement of large masses of the population has been planned for, and in the Evacuation Division there is a medical group, since the same diseases and disorders will go on whether there is war or peace. To conserve the already reduced medical personnel of the State so far as possible, we have frequently utilized physicians for work in both divisions. We have also made arrangements with the Evacuation Division that, should evacuees be so ill as to require hospitalization, they will be turned back to the Medical Division; thus, the establishment of two medical groups to deal with the hospital problem will be avoided.

We still need more first-aid party members and more people trained in first aid to serve in the first-aid posts and as ambulance drivers. The response of physicians and dentists to this effort has been entirely gratifying and satisfactory.

It would be invidious for me to mention any personal names before our colleagues. I have always told His Excellency, Governor Saltonstall, that he need have no fears about the medical aspect of civilian defense, that everywhere in the Commonwealth doctors were happy to help out. It is

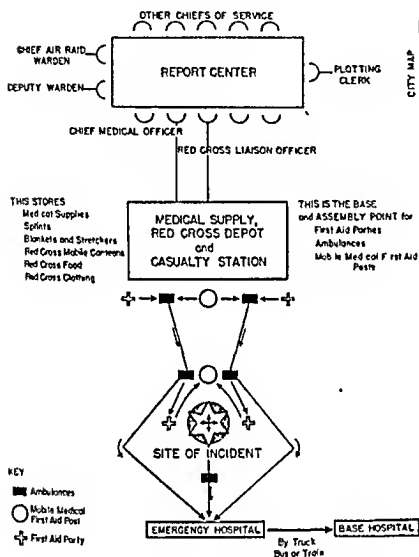


FIGURE 1 Community Organization at and from the Report Center.

ing, thoroughly washed for decontamination, and finally given fresh clothing supplied by the Commonwealth. The intricacy of such a setup, with its gas locks, decontamination and ventilation, need not be gone into here. The Commonwealth has set up an ideal center of this type in the basement of the former Huntington Hospital. This phase of our activities has been under the direction of two physicians, who have not only been willing to go away to acquire an education in this field but also have, in turn, given several courses to doctors of the Commonwealth, so that all communities may be thoroughly instructed in this vital matter. Such decontamination centers should be set up at the rate of one per 100,000 inhabitants. A different handling of patients must be followed when one considers the person who is both injured and gassed. This requires the organization, in the admitting section of each hospital, of a very

now my privilege, however, to thank publicly, though anonymously, those of your colleagues who have shared together in this great effort. It has robbed many of your friends of sleep and income; it has kept them working late into the night when others were at theaters. But it has been a job done for the good of our people, and I congratulate the medical profession for complete and totally unselfish devotion to the common good. The time has now arrived when new efforts are required. The American people, who are naturally optimistic and already misled by unjustifiably hopeful news on the radio and in our newspapers, are beginning to think that we are winning the war and that the end is in sight. This is now leading to defection in the ranks of civilian defense. Air-raid wardens

are less conscious of their tasks, and some are resigning. The cold facts are that we have not won a battle yet. In England, civilians were not bombed until the country had been at war eleven months. Now, as never before, we of the medical profession must stand as a power to keep this essential activity alive and ready for the emergency. We cannot say when disaster will come, any more than the residents of Pearl Harbor or Tokyo could, but we must not underestimate our enemy and we must be prepared lest the women and children of this commonwealth suffer through our carelessness. Every physician who is not serving his country in the military forces should devote a part of each day to this grave and vital responsibility.

THE PHYSICIAN'S ROLE IN FIRST AID*

A. WILLIAM REGGIO, M.D.†

BOSTON

IT is difficult to understand why it took Pearl Harbor to make the medical profession take an interest in first aid, and yet, on the other hand, it is not so difficult. If one faces the question squarely and honestly, one finds two outstanding reasons for this lack of interest on the part of at least 95 per cent of the medical profession: the great majority of medical schools, until recently, have completely omitted the subject of first aid from their courses of study; and physicians are consequently unfamiliar with—and, one might say, ignorant concerning—the subject matter and methods of first aid.

Gradually, physicians are discovering that first aid really amounts to something—that it is not merely childish nonsense or an attempt to turn laymen into doctors in a few short lessons. They are also finding out that the layman expects any physician to be able not only to render first aid in the best and most approved fashion but also to teach the subject to a class at a moment's notice.

Unfortunately, although physicians can diagnose the most obscure diseases and treat the most difficult conditions, when all hospital facilities are available, they are completely at a loss when faced with the problem of administering first aid or transporting a victim to a hospital without the usual equipment.

First aid is not, and must not be considered, a matter too elementary for the serious consideration and assimilation of every physician.

The training of laymen in first aid was begun by the American Red Cross in 1910, when the first class was taught and the first certificates issued, denoting the successful completion of this first course. It took twenty-five years to reach the first million certificates—from 1910 to 1935. Then, for the second million, it took four years, that is, from 1935 to 1939, and the third million from 1939 to 1941, or two years more. During the past year, the fourth million was completed.

In a personal communication, I have just been informed that during the month of March, 1942, Washington issued about 352,000 standard certificates and was still behind in issuing the total number requested. At this rate, if it keeps up, — and it seems to be doing so, — there will be over 4,000,000 standard certificates issued for this year alone. To emphasize this once more: thirty-one years, 1910 to 1941, 4,000,000 certificates; in all probability in this one year, 4,000,000 certificates.

Accordingly, the increased interest shown by the medical profession in first aid, as taught by the American Red Cross, is most encouraging. In January of this year, a short eight-hour course was given to a group of one hundred and twenty-five physicians from the different district societies so that they could transmit this knowledge to others and teach laymen in standard first aid. It was quite evident that all these doctors were pleasantly surprised at what they learned of a subject new to them and that they definitely enjoyed the sessions and profited by them. Since then, the number of doctors asking for instruction in the mechanics of first aid has been most gratifying and encouraging.

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 26, 1942.

†Deputy medical director, Medical Division, Massachusetts Committee on Public Safety.

I shall not mention names, but ten or fifteen doctors in and around Boston have been giving many hours of their time to teaching not only laymen but also physicians and dentists so that they, in turn, could adequately instruct classes of laymen in the standard course. This has not been an easy undertaking, and they are to be congratulated for their perseverance and untiring efforts in doing this job and doing it well.

At long last, a standard course in first aid is being taught to practically all the students at Boston University, Harvard, Tufts and Middlesex medical schools. A large number of these young men have already received certificates as instructors in first aid, and many more are continuing toward that end. The students have taken up this subject with marked enthusiasm, and a number of them believe that the standard course in first aid should be a required part of the first-year curriculum. It is to be hoped that this desire on the part of the medical students will be heeded by the powers that be.

A grievance that it is in the province and power of the profession to dispel is the thoughtless and destructive criticism of first aid still being made by some physicians. Destructive criticism is vicious, constructive criticism is always welcome. It is less than it was a few months ago, but it is still going on and is doing harm by causing confusion in the minds of lay instructors concerning what they are teaching in their courses.

Two main topics are in dispute, namely, the use of iodine in wounds, and traction splinting in fractures.

The application of iodine in a wound is taught in the *First Aid Text Book* of the American Red Cross. Every effort is being made to have this teaching changed so that iodine—in mild, medium or full strength, it makes no difference—will not be used in any wound, and a revision of the text to that effect is advocated.

Traction splinting of fractures. Many physicians still do not appreciate the value of immobilizing fractures before the victims are moved from the scene of an accident to a hospital. The American Red Cross textbook teaches this, and every man familiar with and accustomed to treating fractures agrees with this recommendation. During World War I, the value of this method of transporting patients with fractures, particularly of the femur, from the field to the hospital was amply proved by the facts that before such splinting was instituted the mortality in this type of fracture was about 60 per cent and that after traction splinting was used the mortality dropped to about 25 per cent. This in itself indicates the benefit of this method, to any thinking person. Yet some doctors still oppose or fail to recognize the necessity of this precaution

before moving victims with fractures. Although many laymen who have received certificates for having passed the examination in standard first aid are not capable or willing to apply this method in an emergency, at least they will be able to prevent others from doing the wrong thing to a victim, because they know what should not be done. For example, not very long ago, a victim with a broken lower leg was being prepared for splinting by a layman trained in first aid when a doctor arrived on the scene. The layman naturally gave way to the doctor, who, after some uncomplimentary remarks on the layman's efforts, proceeded to pick up the victim and place him in his car, making the fracture compound in the process. An occurrence of this kind is inexcusable, and should not be countenanced by the medical profession as a body. How can one possibly expect the layman to respect the teaching of first aid when members of the profession so flagrantly disregard the most elementary principles in the care of the injured?

It is readily admitted that certain first-aid measures, as taught to laymen, seem inadequate in the eyes of some medical men, but one must not forget that the layman is not a physician and moreover, that he is not qualified, nor can he be expected, to use some measures that a medical man might be justified in using.

First aid is merely a way for the layman "to hold the fort" without further increasing the damage already done until the services of a doctor can be obtained. Passive inactivity on the part of such a first-aid worker is preferable to active inadequacy, and that is one of the principles taught in first aid. It is better, of course, to do nothing than to do the wrong thing. If the victim is merely left where he is and kept warm until help is available, many a life may be saved.

To play a part in first aid, the doctor must know something about it. Since many physicians are already affiliated with casualty units or mobile first-aid posts and will have working under their direction a personnel trained in first aid, they should be familiar enough with their duties to train these workers in practice sessions, so that in the event of an emergency the unit can function to the best possible advantage.

These people will ask questions that must be answered correctly in the layman's language. One cannot do this unless one can speak the same first-aid language as the personnel. The first-aid workers should not be told to do things that they have not been taught in their courses, and to avoid this confusion it behooves physicians to familiarize themselves with what the workers have been taught.

The commanding medical officer in charge of these mobile units must be able to train his per-

sonnel in stretcher drill. This it will be difficult for him to do unless he has first learned it himself. One hears complaints from many medical men in these units that they cannot obtain a sufficient number of people trained in first aid to act on their units and in the first-aid parties. The demand for instruction is heavy, and the number of lay instructors available is barely adequate to handle the number of applicants.

Hence, if the doctors themselves will instruct the people whom they will have working on their units, the number of trained workers will rapidly increase.

All this, of course, means *work* on the part of the doctors, but as this present emergency progresses, the amount of work will naturally increase; physicians must work even harder than they are doing already, and train their personnel. No one knows when some of the mobile first-aid units will be called on to function as the result of enemy action, and they will be expected to handle the situation adequately. The men in charge of these units and their organization are working day and night to be prepared and ready at a moment's notice. It is imperative that these mobile units hold practice sessions to become accustomed to working together under the tension and confusion that are bound to result if the emergency arises suddenly.

A tremendous responsibility is borne by the medical profession. The public looks to physicians to take care of them in the event of enemy action. Whence or how this will come is not known, but one certainty is that the emergency *will* arise and that physicians must be ready to cope with it and render the best possible care to the injured.

As more doctors leave civil practice to enter the Army or Navy, increased work is thrown onto those remaining behind. Mobile medical units already formed must find new men to replace the ones called to active duty. Such new men will have to be trained for this first-aid work, and it will help tremendously if all physicians look ahead even farther and acquaint themselves with what is going on in their communities and find out where they will be most needed and best fitted to serve.

Everyone should be familiar with the measures that are to be carried out at the medical first-aid posts or casualty stations throughout the State, and with the measures to be taken in the event of chemical or gas warfare as affecting the civilian population.

When the emergency actually arises, it will be too late to learn, and there has already been enough of "too little and too late." We cannot afford any more delays. We *must* anticipate the next play and be ready to checkmate it from the very start.

At the first-aid casualty stations, which will be set up as near the scene of an incident as possible, only the most essential first aid will be rendered to the casualties. Any major procedures will be carried out by the emergency teams at the hospitals to which victims are taken by ambulances from these medical posts. It is therefore necessary for the physicians comprising the personnel of these posts to be thoroughly familiar with such measures as the splinting of fractures for safe transportation.

They must be able to guide their first-aid helpers in the application of these splints, whether for immobilization or for traction. The control of hemorrhage is vital, and decisions concerning the application of a tourniquet must be made rapidly; correct application is essential and will be the responsibility of the physician in charge.

His familiarity with emergency procedures is vital, since he is the one who must keep calm and cool so that his assistants will not become panicky or disorganized in the face of conditions of suffering and injury that they will encounter, in actual fact instead of in theory, during their course of instruction. The physician is accustomed to sights and sounds that will be entirely new to the layman; it will be his responsibility to keep things running smoothly.

He must be familiar with artificial respiration, which is not so easy and simple as it sounds. Practice and experience in its administration are necessary before it can be done correctly and efficiently. Burns will have to be taken care of and quickly sized up as to severity, and appropriate first aid given with the materials at hand before the cases are sent to the hospital. Morphine must be given in sufficient dosage to quiet a victim during transportation. Judgment regarding the size of the dose is necessary to make sure that it is large enough to accomplish its purpose. Shock treatment of an elementary kind must be given to tide over the victim until he receives further treatment at the hospital. Major and minor wounds must be evaluated rapidly, and the danger of minimizing an injury must be avoided — especially in head injuries is this danger very great, as, of course, everyone knows. Underestimating the potential complications in head injuries may be fatal, whereas a more mature appreciation of possible underlying injury may make a tremendous difference. This is well known, but is worth emphasis.

* * *

To conclude, I again emphasize the importance of the physician's role in first aid — the layman looks to us for guidance and instruction. How can we possibly help him to the best advantage if we, ourselves, are not thoroughly familiar with this subject?

374 Marlborough Street

MEDICAL-SCHOOL PLANS FOR THE EMERGENCY*

BENNETT F. AVERY, M.D.†

BOSTON

AT a time when our very survival depends on an immediate all-out military effort, any civilian activity whatsoever must justify its right to continue. We have suddenly awakened to the startling fact that one plane or gun or ship now is worth ten next year and a hundred the year after. We are newly aroused to the necessity of throwing everything we have into ensuring that we do not lose the war this summer, and at the same time we are filled with the dawning hope that if we work hard enough and move fast enough we may achieve victory in 1942.

Nothing can have precedence over the priority that we must accord to the military effort, and it is in the light of this fact that we should examine the situation regarding medical education. We should consider not only the effect of the war on the medical schools but also the contribution the schools are making or can make toward winning the war.

It is now clear that, of the 155,000 practicing physicians in the country, 30,000 will soon be in the medical corps of the Army and Navy. It is conceivable that in a prolonged war this number might even be doubled. The effect, as you all know, is already being acutely felt in communities and hospitals. It will be far worse before it gets better. Every available young physician will soon be in active service, and if the war should take longer to win than we hope, there may not be enough who are physically fit to meet the needs of the military forces.

The inescapable conclusion is that it is the duty of the medical schools not only to continue in operation but to train capacity classes as rapidly as is consistent with the maintenance of high standards. This was early recognized by the three schools in Massachusetts, and on December 29, 1941, Tufts College Medical School, Harvard Medical School and Boston University School of Medicine issued a joint announcement to the effect that beginning July 1, 1942, summer vacations were to be eliminated in favor of a program of continuous operation.

To consider the many problems involved in the adoption of accelerated schedules, a special meeting of the Association of American Medical Colleges was held on February 14 of this year in connection

with the Annual Congress on Medical Education and Licensure of the American Medical Association. The program was approved in principle for those schools that could adopt it without sacrificing teaching standards. Resolutions were passed at this time by the Council on Medical Education and Hospitals of the American Medical Association and by the Federation of State Medical Boards of the United States supporting the action taken.

The result has been that up to the present fifty-nine of the sixty-seven four-year medical schools in the United States have adopted an accelerated schedule, and four more are expecting to adopt one. In most cases, classes are to be admitted every nine months, beginning about July 1, 1942, and the four academic years will be completed in three calendar years. This means a 33 per cent speed-up in the production of physicians, showing its first fruits next February and March, when five thousand doctors will graduate three months earlier than normal. The following January, another five thousand will graduate six months early, and in September, 1944, a third five thousand will graduate nine months before the regular date. The climax will come at the end of three years, when a class of five thousand will finish a year ahead of the normal time.

The difficulties involved are great, but are no worse than those attending most phases of the war effort. Hospitals, faced with providing internships at nine-month intervals, have proposed making their old interns who have served nine months into junior residents for their remaining three months, to supervise the newcomers. The expected dearth of residents will make this feasible.

In seven states, the medical-practice acts require a recognized medical course to be given in four different calendar years, but amendatory legislation is under way or expected. In five other states, the law may be liberally construed as it stands. In the remainder, the question is for the examining board or other state approving agency to decide, and in view of the action taken by the Federation of State Medical Boards, no trouble is anticipated.

Almost universal action on the part of pre-medical colleges in adopting an accelerated schedule of their own will probably maintain a full supply of applicants for admission at the irregular nine-month intervals. My own observation has been that most applicants for places in the incoming class of next March expect to complete a full year's

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†Dean and Waterhouse Professor of Anatomy, Boston University School of Medicine.

work between now and then, by taking a double summer session in addition to the regular fall semester.

The substitution of a short rest period between each academic year in place of the long summer vacation raised the question of financial aid to students who were formerly dependent on summer earnings. The generous action of the W. K. Kellogg Foundation in making available loan or scholarship funds to one hundred and fifty medical, dental, public-health and nursing schools in the United States and Canada has helped greatly in meeting this urgent need, and private donors have been generous. It may even be that a government loan fund will be established for succeeding years.

There is still the question how well the health of the students will stand the strain of continuous cycles of eight months of work followed by only one month of vacation, but plans are under way for an unusually careful watch over their physical condition. It is hoped that breakdowns due to tuberculosis or mental or nervous fatigue will not increase unduly.

The War Department, the Navy Department and the Selective Service System have recognized the need for maintaining a constant or increasing flow of graduates from the medical schools by deferring students in good standing almost without exception. All medical students and even those accepted as members of the next incoming class are now eligible for commissions as provisional ensigns in the Naval Reserve or as second lieutenants in the Medical Administrative Corps of the Army. In the latter event, not even a physical examination is required. All students commissioned are assigned to the study of medicine until they shall have completed their course and one year of internship.

So far as the faculties are concerned, the situation is difficult. Every school has lost large numbers of its younger staff members, but an effort has been made by the Procurement and Assignment Service to leave key men who are essential to teaching. Those remaining are carrying increased loads because of the smaller staff and accelerated schedule, with resultant sacrifice of research and vacation time. Even so, throughout the country, numerous members of the medical-school faculties are carrying on full-time or part-time research on special war problems, at the request of the National Research Council.

The teaching of military medicine has been given careful consideration, and proposals have been put forward by a special committee of the Association of American Medical Colleges, composed of Dr. Edwin P. Lehman, chairman, Dr. Currier McEwen and Dr. H. S. Mustard. It is

suggested that, except in schools where a reserve-officers training corps is already established, there be no attempt to teach the organizational aspects of military medicine to undergraduates, unless it is for a brief course of orientation lectures.

It does seem desirable, however, that beginning in July, the first-year and second-year students who have not had first-aid training be given at least a twelve-hour course of lectures and practical work. Tropical medicine should be stressed in courses in parasitology and medicine, or even as a separate course in the clinical years. Discussions are now under way for the establishment of such a course as a co-operative effort of the three medical schools in Boston.

To quote the report of the committee:

The necessity for stressing certain subjects of the professional aspects of military medicine within the framework of the present curriculum is recognized. These subjects include the following:

- Shock and blood substitutes
- Soft tissue wounds (including débridement)
- Fractures
- Burns
- Frost-bite
- Sanitation
- Control of communicable disease
- Prophylaxis and treatment of venereal disease
- Cardiovascular disease
- Fatigue states
- Anoxemia
- Compression and decompression
- Acroembolism
- The physiology of high altitudes and dive-bombing
- Visual adjustments under war conditions
- Poison gases
- Industrial poisons
- Common psychiatric conditions, including modified peptic ulcer syndrome and effort syndrome
- Dermatoses and insect bites

It is recommended that a special course on the professional aspect of military medicine be given to fourth-year students, to include any material listed which has not been previously given and any new material developing as the result of present war experience, such as the newer treatment of burns, the developments of sulfonamide therapy, immersion foot, blast injuries, renal failure of crush injuries, etc.

Even the faint possibility that we may suddenly need to evacuate certain of the medical schools that are located near the seacoast to safer districts inland has been considered. Tentative plans are being laid for removal to districts offering facilities not only for the schools but for the hospitals used in clinical teaching. Any possible arrangement would be far from ideal, but even though we confidently expect that no one will have to move, it seems best to be prepared, for once.

* * *

In conclusion, let me say that once again the medical profession has shown itself to be one of

the most patriotic and foresighted groups in the country. There seems to be no tendency for a brass-hat regime to obstruct swift and decisive action,

and every medical school in the country is making every possible contribution to the war effort
80 East Concord Street

HOSPITAL PREPAREDNESS*

CHARLES F. WILINSKY, MD†

BOSTON

THE country is at war. The long accepted theory of safety and protection afforded by distance has been thoroughly shattered, and to day the Atlantic and the Pacific oceans are no longer the protective barriers they were so long believed to be. It has been wisely concluded, therefore, that the whole country must be thoroughly organized for the defense of its population.

Much has been said and a great deal written about the place of the hospital in civilian defense. It requires neither particularly keen vision nor vivid imagination to appreciate in its fullest form the vital part that hospitals will be obliged to play in the drama of life and death that sabotage and war, if brought to these shores, will produce.

Modern warfare exacts a tragic toll, not only in a high percentage of deaths resulting from demolition and incendiary bombs, but also in serious injuries, whose treatment requires a high quality of surgical skill.

To meet these possible needs, the Medical Division of the Office of Civilian Defense was created in Washington and placed under the able direction of Dr. George Biehr. The necessity for the formation of state units was urged, and Massachusetts, in keeping with the richness of its traditions in the field of social consciousness and human welfare, was in the forefront of this essential development. We were particularly fortunate in the sacrificing willingness of Dr. Elliott C. Cutler to give so much devotion to the office of director of the Medical Division of the Massachusetts Committee on Public Safety.

Others who have spoken on this program have described the organization of the medical services, with their mobile units, which include physicians and other essential personnel. The establishment of first aid posts near the scene of the incident, as well as medical depots and casualty stations, has been described. Fitting emphasis has been placed on the type of essential organization for the proper functioning of the groups mentioned above, and the services they are expected to render.

It is pertinent to call attention to a certain variance in the functioning plan for medical services in Massachusetts, as contrasted with the recommendations of the Medical Division of the Office of Civilian Defense in Washington. The plan of the latter includes the organization of medical field services from the nonsurgical resident staffs in hospitals, whenever possible. Among the important justifications claimed for this plan are the speed of mobilization and the economy of manpower. The plan in Massachusetts, for which Doctor Cutler is responsible, is built on the premise that hospitals should keep their staffs intact, to care for the injured brought to their doors. The medical field services are to be rendered by practitioners of medicine, recruited in the main from the areas in which they practice or reside and in which they are expected to serve at the time of the emergency.

In the planned organization of medical services, it is readily recognized that emergency hospitals must be made available for the care of the more seriously injured. Nearly one hundred hospitals in Massachusetts are intended to serve as emergency hospitals and are closely linked with their local civilian-defense organizations.

One could devote many pages to the specific recommendations that have been presented for the physical protection of hospitals, including buildings, personnel and patients. However, various factors intervene that must receive careful consideration in the development of local plans. It is, nevertheless, possible to agree on certain objectives, which may be considered the minimum goal of all hospitals.

Protection of Physical Property

The first objective is adequate protection of the physical property of the hospital against damage caused by sabotage, explosion, demolition and incendiary bombs, fires and so forth. This protection can best be accomplished by the installation and maintenance of adequate blackout facilities; adequate protection against fire, organization for necessary emergency repairs to the hospital structure, including possible damage to heat, light, water, power, structural damage and so forth,

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†Lecturer, Department of Biology and Public Health, Massachusetts Institute of Technology; executive director, Beth Israel Hospital; deputy health commissioner, City of Boston.

and the necessary protective mechanisms for safeguarding patients and personnel, including the organization of rescue squads, provision for air-raid shelters and so forth.

The maintenance of blackout facilities involves the expenditure of funds for blackout material and the cost of installations.

Protection against fires caused by sabotage or incendiary bombing compels the organization and drilling of fire squads recruited from employees as well as volunteers. A carefully selected fire warden trained particularly in the art of handling incendiary bombs will in turn impart this knowledge to spotters and fire fighters. The need of constant watchfulness is a major factor in protection against and control of fires.

The maintenance department of the hospital must concern itself with the problem of emergency lighting and particular protection of the telephone service, water supplies and the power and heating plants. The purchase of auxiliary equipment to meet these needs in the emergency is a justifiable expenditure.

An adequate amount of essential supplies must be provided, and it is strategically sound to store these supplies in several places in the hospital, rather than to expose a concentrated supply to the hazard of destruction. Safe storage should be provided for alcohol, ether and other chemicals. A census has been taken of radium owned by Boston hospitals, and advice given regarding safe storage.

The safety of patients and personnel should be given primary consideration. None of the methods suggested for the protection of glass, including windows and skylights, can be considered foolproof. Wire netting, cloth and beaver board are but some of the suggestions. It is, of course, logical that at the time of bombing, patients and others be moved away from proximity to glass windows. Corridors appear as reasonable shelters as any other places that have been suggested.

Included in the mobile-unit organization radiating out of every medical depot are Red Cross ambulances and, when necessary, other vehicles provided by the chief medical officer. These will be used for the transportation of patients to hospitals on orders of the physician in charge of the first-aid post.

Care of Casualties

The second objective, the development and maintenance of facilities for the prompt care of casualties, must include adequate space and a well-organized plan for the reception of the injured, and the exercise of proper judgment concerning the disposition to be made of the victims, in accordance with the degree of the injury, and their needs.

This calls for continuous, essential, well-equipped professional service, including the availability of surgeons, nurses, anesthetists, x-ray and laboratory units, transfusion facilities and shock teams. It is essential to re-emphasize the need of personnel on a twenty-four-hour basis.

One cannot overestimate the value of the prompt and sound sorting, by the triage officer, of the injured brought to the hospital, and the careful recording of the disposition of the cases. The skillful surgeon assumes a serious responsibility for the making of important decisions concerning: disposition of the walking wounded; patients in need of immediate surgical attention in the operating room; treatment for shock; need of x-ray diagnosis of fracture, foreign objects and so forth; treatment of burns; fracture service; and specialized services, including the orthopedic, eye, nose and throat, neurosurgery, faciomaxillary and those for the treatment of serious chest and abdominal wounds. Doctor Cutler wisely advises constant watchfulness, so that the secondary needs of casualties sent first to the above units may be adequately met. Leadership and authority should be vested in the executive director of the hospital.

Plans must be developed in every community, to assure a working knowledge of the number of available beds for the care of casualties. In communities with a number of hospitals, a central registry of hospital beds must be established, to which the regional and chief medical officers, as well as hospital authorities, will have access for necessary information. At the time of the incident, the medical officer or his deputy will be at the control center, and in possession of this essential information. He will be in periodic touch with hospitals and the deputy medical officer in charge of medical depots and their mobile units. It will be possible, through this constant vigilance, to send victims promptly to the emergency hospitals that have available beds.

In determining the availability of beds for the care of casualties, certain major factors must receive primary consideration. These include the number of available surgeons, nurses, physicians, anesthetists, shock teams and x-ray personnel. The number of available operating rooms is a vital consideration. One must give serious thought to Doctor Bachr's admonition not to overcrowd the individual hospital. He places particular stress on the fact that very few hospitals could adequately care for more than 50 casualties in twenty-four hours. The whole question of adequacy of supplies, including stretchers, blankets, splints, plasma and tetanus antitoxin, must receive proper consideration. It is pleasing, indeed, to pay tribute to the hospitals in Massachusetts that have spent substantial sums for adequate preparation to meet

possible demands made on them at the time of the emergency. Supplies have also been provided, and more are to come from state and federal sources.

Facilities for Evacuation

The availability of beds for casualties is dependent on the organization of sound methods for the evacuation of patients. These include: discharge of convalescents to their homes, nursing and convalescent homes, and other designated places, discharge of wounded patients not requiring hospitalization to the places designated above; and evacuation to base hospitals.

In the event of extensive recurrent bombing, as well as of serious damage to emergency hospitals, it will be necessary to evacuate patients extensively to base hospitals.

Elaborate plans have been developed on a statewide level for the establishment of base hospitals. It is planned to use state sanatoriums for tuberculosis, mental hospitals, institutions under the Department of Public Welfare and, possibly, federal hospitals. Plans for supplemental staff organization are in the process of development. The transfer of wounded from local emergency hospitals to base hospitals is the responsibility of the Women's Defense Corps of the Massachusetts Committee on Public Safety. Arrangements for such transfer will be made by the chief medical officer on request of the representative of the emergency hospital. The medical officer will relay this request to the regional medical officer of the district, who will take the necessary steps for the arrangement of such evacuation.

Requests for the evacuation of patients from the emergency hospitals to their homes will be made to the chief medical officer, who will arrange for needed transportation through the American Red Cross.

Regional hospital officers and a state hospital officer have recently been appointed. Among the functions of the latter are studies of existing hospital resources, including base hospitals, methods and routes for prompt transportation from emergency to base hospitals, essential staff and equipment, and needs.

Decontamination

The subject of decontamination of patients suffering from chemical warfare is of serious concern to hospitals. Emergency hospitals are expected to provide facilities for the decontamination of patients, particularly of the type suffering from both gassing and injury. It is recommended that such facilities be built or made a part of the admitting unit of the emergency hospital.

The decontamination unit should ideally provide for three rooms, thus making the following possible: room for removal of contaminated clothing, room for washing and other essential decontamination treatment, and room for clothing of patients and emergency treatment of wounds. For their protection, attendants should wear masks, gas-proof gloves and clothing. It has been strongly emphasized that decontamination of the patient must be carried out before admission to the hospital for treatment.

* * *

In this description of the place of the hospital in civilian defense and the present status of hospital preparedness, it is fitting to call attention to the problems that the war has created for the hospital structure. Staffs have already been materially depleted. The nursing shortage is constantly increasing, and lay employees are frequently preferring the more lucrative opportunities that industry offers. The needs of the Army and Navy, however, must be met, and the war must be won. Many physicians who have retired from hospital staffs are gladly coming back to fill the gaps created by those who have gone into the Service. Nursing aides are rendering invaluable help in replacement of nurses who have enlisted. Volunteers, who deserve unstinting praise, are frequently taking the place of paid personnel.

In sections of the country where the staffs of hospitals are expected to play the double role of providing for medical services in the field and in the hospital, — and here in Massachusetts, where they are so willingly organizing themselves to care for the injured brought to their doors, — there will be much to do in the event of hostile penetration of our shores.

To the glorious heritage of the hospitals of America, which have grown from a modest total of 150 hospitals less than sixty years ago to their present imposing number of over 6500 institutions, is now added the opportunity for service to the civilian population, exposed to the possible hazards of war brought to their own hearthstones. In planning for the efficient functioning of our hospitals in these times of great stress, one may learn much from the bitter experiences of the hospitals in England. Bitter, however, as was their tragic lot, we salute their indomitable will for service, and we glory in their refusal to be conquered. We join with them in this great privilege for service to our neighbors, in this great enterprise with freedom our goal and, God willing, our reward.

330 Brookline Avenue

MEDICAL PROGRESS

DIAGNOSTIC ROENTGENOLOGY: DANGERS ASSOCIATED WITH FLUOROSCOPY*

RICHARD SCHATZKI, M.D.†

BOSTON

IT is likely that the opportunity for x-ray injuries will increase during wartime. In spite of the efforts of the Army and Navy to use specialized, well-trained radiologists, it can be assumed that quite often fluoroscopies of fractures, as well as fluoroscopies in the search of foreign bodies, will have to be performed by men who have had no, or inadequate, training in radiology, and the possibility of injuries exists. Such a danger appears so imminent that this report is devoted exclusively to its discussion.

Every physician remembers, either from his own experience or from the description of others, the extensive injuries produced by x-rays in the first few years after their discovery. At present, x-rays are used so extensively for diagnostic work and injuries seem to have become so rare that it may appear as if x-rays had lost their dangerous qualities. It is true that in many ways modern equipment is safer than that used in the early days of x-ray investigation. The danger of electrical shock no longer exists in modern shock-proof apparatus. Shielding has, in modern types of tubes, eliminated the radiation that formerly escaped from the old glass-bowl type of tube into the examining room outside the field defined by the shutter. But these improvements have not changed the inherent biologic qualities of x-rays. The rays used for the actual examination are still the same that killed a large part of the first generation of radiologists. Owing to technical improvements and particularly to increased knowledge of the inherent qualities of x-rays, the proper application of these rays is no longer dangerous; however, if used excessively and indiscriminately, they obviously will still produce damage. Evidence is accumulating to show that in recent years there has been a disquieting increase rather than a decrease in the number of skin injuries resulting from the use of x-rays.

From 1938 to 1941, Uhlmann¹ saw 70 patients with radiation injuries to the skin. In 40 of these cases, the injuries resulted from the use of x-rays

for diagnostic or technical purposes; only in 30 cases were the injuries caused by x-ray or radium treatment. (Fourteen, or about half, of the latter had been treated for nonmalignant lesions!) There were 27 physicians, 4 dentists and 4 physicists among this group of 70 patients, but only 3 of them were radiologists, and they had been exposed to radiation from twenty to forty years. Of the remaining 32, 28 attributed their injuries to diagnostic work: 4 dentists had been accustomed to hold the films in the patient's mouth during the exposure, 4 physicians had been injured while attempting to remove foreign bodies, and 2 pediatricians had been in the habit of holding babies behind the fluoroscopic screen. Among the non-professional patients, only 6 had been treated by a trained radiologist. In no case was a radiologist responsible for injuries occurring in the course of diagnostic procedures. Uhlmann emphasizes the high percentage of injuries in physicians due to diagnostic work—a fact that he ascribes to a variety of causes, including “unsatisfactory equipment, inefficient protection, inadequate knowledge of the dangers involved, or simple carelessness, since in some instances the injurious effects are unquestionably due to inexcusable disregard of protective measures.”

Leddy and his co-workers,²⁻⁴ in several papers, have stressed the bad effects that result from indiscriminate use of x-rays. From 1919 till 1939, they saw 235 physicians with definite radiodermatitis. Eighty of these physicians were seen within the last six years of this period. The serious character of the radiodermatitis in these physicians is emphasized by the fact that almost 50 per cent of them had either epitheliomas or ulcers due to radiation. In at least 101 cases the damage was attributed to exposure during fluoroscopy. There were only 8 radiologists among the total group, and in only 4 of these was the damage due to fluoroscopy. Leddy and his co-workers found the following main causes of injury: carelessness in the handling of radium and radon—a minor factor; needless exposure of the hands during radiography, for example, in the taking of dental films, the performance of radiopaque injections, the holding of difficult patients and of children, and the holding of cassettes in the preparation of complicated

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. \$4.00).

*From the Department of Radiology, Massachusetts General Hospital.

†Instructor in roentgenology, Harvard Medical School; radiologist, Massachusetts General Hospital.

radiograms; and poorly performed fluoroscopy. As stated above, the last was by far the most important factor. Further investigation showed that none of the physicians in question used lead rubber gloves regularly, and about one third of them used no protective devices whatever. The most dangerous fluoroscopic methods were removal of foreign bodies and reduction of fractures.

Two outstanding facts in Leddy's papers should be emphasized. One is the markedly increasing number of physicians with radiodermatitis whom he had seen in recent years, and the other is the small number of trained radiologists among his patients. Leddy and his co-workers believe that this merits "serious consideration by those who think that roentgen technique is easily acquired and is safe." They add, "The risk involved in the casual use of the roentgenoscope by those without special training cannot be emphasized too strongly, for mechanical equipment cannot be substituted for mental equipment in any branch of roentgenology."

Scheele and Cowie,⁵ who recently reviewed the irradiation protection in 45 hospitals, 32 of which had more than two hundred beds, describe the large amount of radiation to which the technicians in some of the departments were exposed, usually because of their own carelessness. One of them received 35r while holding a single patient—about one hundred and seventy five times the dose that is considered safe as a daily exposure. Exposures during fluoroscopy, however, were found to be the most excessive ones in this survey, and strong measures to reduce this risk were recommended. In contrast to the findings of Leddy and his co-workers, Scheele and Cowie saw skin damage in 12 out of 60 radiologists. The high incidence found in this survey is probably explained by the fact that finer skin changes were included among the 12 physicians, although epitheliomas were seen in some of them.

To these reports of the recent literature, I should like to add two personal experiences that may illustrate the situation. A few years ago I saw a young physician who had been an intern in one of the large hospitals of this country. One day, a patient with a difficult fracture of both bones of the forearm entered the hospital. While trying to reduce this fracture, the doctor used a shockproof portable unit. He had had no particular training in roentgenology and thought the machine was perfectly safe. Because the unit was shockproof, it was possible for him to put the patient's arm close to the tube, and he soon discovered that by so doing his fluoroscopic light was much brighter. Not satisfied with his reduction, he tried again the next morning and fluoroscoped exten-

sively. The results of these two fluoroscopies were bad burns for both the patient and the doctor. When I saw the doctor, he had lost the terminal phalanges of two fingers, and had severe radiation damage of two additional fingers of both hands (see Fig 11 Daland⁶). In other words, extensive burns are still possible from the use of x rays in the examination of a single patient, if the examination is not done with the necessary precaution.

The following event, which happened recently in Boston, demonstrates the degree of ignorance that may be combined with the possession of x ray equipment. A physician called up a salesman of x-ray apparatus, told him that he was dissatisfied with his x ray equipment and wanted some machine that would not burn. A surgeon might just as well ask for a knife that would not cut!

In summary, one may say that (1) x ray injuries still occur, and there is evidence that they are increasing in number in recent years; (2) that a large number of x ray injuries occur during diagnostic examinations—it is even likely that, at present, more injuries occur from such procedures than from the therapeutic application of x-rays, (3) that modern shockproof x ray equipment does not prevent the occurrence of x ray injuries and, although of great advantage to the skilled worker, is, if used unintelligently, in some respects even more hazardous than the old, nonshockproof equipment, because it allows a dangerously close approach of the patient and of the doctor's hands to the x-ray-producing target⁷, (4) that the commonest cause of injuries is the inadequate knowledge of the examining physician, who does not know enough about the technical setup of his equipment and does not realize the dangers that may involve the patient and himself—the second commonest cause is carelessness, and (5) that severe injury to the patient and the physician may occur from a single faulty examination.

How can radiation damage be avoided? Fluoroscopy is the outstanding cause of radiation injury, and is of the greatest consequence in fracture and foreign body work, particularly during wartime. Further discussion is therefore confined to the elimination of fluoroscopic hazards. The safest way of avoiding injury is the complete omission of fluoroscopy. The British Emergency Medical Service⁸ has circulated a memorandum to all medical officers in which it emphasizes the danger of poorly performed fluoroscopies. According to this memorandum, fractures and foreign bodies should be fluoroscoped only in exceptional cases. The advantages of fluoroscopy are, however, too great in many cases for it to be omitted, but it should be performed by a roentgenologist whenever possible. If this is not feasible, the examining

doctor should be instructed and supervised by a roentgenologist, who should also examine the technical equipment. Furthermore, whoever does fluoroscopy should realize that the danger of radiation damage exists, that the amount of danger is in direct proportion to the amount of exposure, and that it can be avoided.

What is the safe dose to which the patient can be exposed? The dose should be smaller than that which will produce an erythema of the skin—less than approximately 300 r for the type of radiation in question. Because of the variation that may occur in the output of any diagnostic x-ray equipment, not more than half this dose can be considered safe. The output of different machines varies, and can be determined only by actual measurement. Measurements at the Massachusetts General Hospital, performed by Mr. Oliver E. Merrill, showed a variation between 14 and 25 r per minute, measured on the tops of different fluoroscopic tables. The distance of the table top from the target of the x-ray tube varied between 34 and 39 cm.; the measurements were made with 80 kilovolts and 4 milliamperes. In other words, with the setup in this department, actual fluoroscopic time from six to ten minutes can be considered safe, the time varying from machine to machine. It is obvious that this dose should not be repeated frequently at short intervals.

Increase in milliamperage increases the amount of radiation correspondingly. Decrease in the target-skin distance increases the amount of radiation by the square of the distance: that is, if the distance between the target and skin is only 20 instead of 40 cm., the amount of radiation will be four times larger. Insufficient realization of this law is one of the common causes of injuries, especially in modern shockproof equipment, which enables one to come close to the target. Actual measurement shows that 462 r per minute are delivered by the tube of a shockproof portable machine if the ionization chamber is in contact with the tube; in other words, the safe dose defined above at this distance would be delivered in twenty seconds.

Which dose can be considered safe for the examining physician? It is obvious that it must be much smaller than the dose safe for the patient, because of the repeated exposures to which the operator is usually submitted. Never, under any circumstances, should the palpating hand or any other unprotected part of the examiner's body be in the direct beam of the x-rays. The importance of this rule cannot be overemphasized. However, the examiner cannot avoid being exposed to a certain degree of so-called "scattered rays," which are produced secondarily by objects in the direct beam. Every fluoroscopic room shows some scattered radiation,

which can be demonstrated by the use of a portable fluoroscopic screen or by small dental films, and can be measured accurately by the ionization chamber. It is obviously difficult to determine the amount of exposure to scattered radiation that can be considered safe. Answers to inquiries made by investigators in various countries among roentgenologists who for many years had been exposed to scattered radiation vary in the amount of so-called "safe scattering." The majority of the investigators believe that 0.2 r daily exposure of the total body will do no damage. Scattered radiation is quite unimportant when the dangers connected with fluoroscopy of fractures and foreign bodies are considered. If damage is done by these examinations, it is caused by direct irradiation.

The necessary protective measures are as follows:

Equipment. It is assumed that standard modern equipment is available for the examiner. The tube is shielded and probably shockproof. A filter is in the tube, and if actual measurement shows too large an output, another filter should be added.

The fluoroscopic equipment should include a shutter with which the direct beam can be reduced to the actual size needed. The fluoroscopic screen should be rigidly connected with the tube and should be large enough so that it will be difficult or impossible for the direct beam to go beyond the confines of the screen. A lead glass of sufficient thickness should be in front of the screen. The patient should be placed so that there is a safe distance between his skin and the target of the tube. As described above, the intensity of x-rays decreases with the square of the distance. The output of the x-ray machine varies with the amount of milliamperage and voltage. If 6 milliamperes are used, the output will be one and a half times as much as that with 4 milliamperes. Increase in the kilovoltage from 80 to 90 will double the actual exposure on the patient's skin. The sides of the machine should be constructed so as to emit as little scattered radiation as possible. A primary cone, which is a cone attached to the x-ray tube, is of particular advantage for this purpose. This cone should come as close as possible to the top of the table on which the patient is examined.

Fluoroscopic Technic. Fluoroscopy is an art. The greater the care with which it is performed, the better the results and the less the danger for patient and examining physician. Fluoroscopy should be performed in a completely darkened room. The examiner should not be disturbed by any outside light entering the room at any time. A red light should be connected with the foot switch

so that it will turn on automatically when the current of the machine is interrupted. The examiner should adapt himself with dark glasses, or by sitting in a darkened room, for at least fifteen minutes. To overcome poor visual adaptation by an increase in the tube current is a poor policy. Such a procedure does not compensate for the loss of diagnostic acumen and represents an inexcusable increase of the fluoroscopic risk. An excellent description of physiology and practice of adaptation is given in a recent article by Chamberlain.⁹ Simple ways for testing the optimal degree of adaptation are outlined. In the same article, Chamberlain prophesies the application of the principles of television and ultramicroscopy for fluoroscopy. By amplification, unheard of brilliancy of the fluoroscopic light would result, which would minimize the risk of fluoroscopy and revolutionize roentgenology.

The actual fluoroscopic exposures should be as short as possible. The current should be shut off when it is not actually needed for observation—for example, during discussions or demonstrations. A shutter should be used to define the fluoroscopic field. Keeping the shutter opening as small as possible has a threefold advantage: it improves the fluoroscopic image and decreases the danger to the patient and to the doctor.

Since any handling of a fracture during fluoroscopy markedly increases the risk of the examination, fluoroscopy should be used only to check an obtained position. As emphasized above, the hand of the examiner should never appear in the direct beam of the x-rays. He should wear lead rubber gloves and a lead rubber apron.

Measurement. The actual amount of x-rays to which patient and doctor are exposed should be measured by an ionization chamber. Wherever this is not possible, and I can think of many places where it will not be, particularly under war conditions, the machinery should be carefully checked as outlined above, if possible by a physicist or a roentgenologist, for protection against overdosage and correct definition of the direct beam. The scattered radiation can be fairly easily demonstrated with the help of dental films, which are placed at various exposed areas or, simpler still, with the aid of a portable fluoroscopic screen. A small amount of fluorescence will be present in any fluoroscopic room, owing to the scattering. A leak in the protection, however, can be readily discovered by the

locally increased intensity of light seen on the portable screen, and the leak can be obliterated.

Personnel. The attitude and training of the examiner are the most essential factors in the protective scheme. A well-trained, conscientious examiner can use obsolete equipment safely, whereas an ignorant or careless worker can do irreparable damage with the most modern equipment. An adequate fluoroscopic technique can be learned only through personal teaching. Good descriptions of fluoroscopic technique¹⁰ are helpful but they are not substitutes for such personal training.

Physical data regarding protection, more extensive than those presented in this review, can be found in a number of recent publications.¹¹⁻¹³

* * *

Modern x-ray equipment does not prevent x-ray injuries. In some respects, it is even likelier than old-fashioned machines to produce damage, if used without the necessary knowledge. There is evidence that in recent years there is an actual increase in the number of persons injured by diagnostic procedures. The physician who "does a little x-ray work" is in greater danger than the expert roentgenologist, and it is he who needs protection.² Whoever uses x-ray equipment, particularly for fluoroscopic purposes, should realize the danger to which he exposes the patient and himself, and he should be certain that all possible points of danger have been eliminated, otherwise, serious damage may result.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28271

PRESENTATION OF CASE

A sixty-year-old unemployed carpenter was admitted to the hospital because of cough of five months' duration.

Two years before entry, the patient fell, striking his lower right chest against a stake. A roentgenogram was said to show questionable fracture of the eighth rib near the spine. After this, the patient began to have periodic pain in the region of the right nipple, occasionally radiating through to the back, to the right side of the neck and occipital region, or to the right axilla and right upper arm. These attacks occurred once or twice a week, and frequently accompanied damp weather or the lifting of heavy objects. The pain was sharp and intermittent. The patient was otherwise well and was able to continue his work. Eight months before entry, there was some loss of appetite. Five months before entry, there was gradual appearance of cough productive of two or three tablespoonfuls of white sputum. The attacks of pain were aggravated by the cough. After a few weeks, the patient began to feel nauseated. Attempts at vomiting increased the cough. The sputum became foul, leading the patient to consult a physician. A roentgenogram of the chest was said to show "clouding of the right lung." The patient was given *green liquid medicine* and white pills. He remained in bed for about a month, with some resultant improvement in his general condition, and then returned to work. The sputum became increasingly foul and turned green. Two and a half months before entry, the sputum became pink, up to half a pint a day being raised. Gradually, the sputum became frankly bloody. Two months before entry, the patient was forced to stop work because of shortness of breath. There was a weight loss of 10 or 15 pounds in the course of the illness.

The past and family histories were irrelevant. Venereal disease was denied.

On admission, examination showed a poorly nourished, chronically ill man of middle age, coughing and orthopneic. The veins over the neck and arms were prominent, more so on the left than on the right. The heart was of normal size, with a rough systolic murmur at the aortic

area, poorly transmitted to the neck. Coarse rales were heard throughout the right chest, with occasional loud expiratory squeaks and groans over the right upper lung field. There was dullness over an area corresponding to the right upper lobe anteriorly, posteriorly and in the axilla. Breath sounds and vocal and tactile fremitus, however, were not altered in this area. A few small cervical lymph nodes and a solitary left supraclavicular node were palpable but not tender. The liver edge lay just below the costal margin. The abdomen was otherwise normal. There was early clubbing of the fingers. Neurologic examination was negative.

The blood pressure was 110 systolic, 55 diastolic, in the right arm and 105 systolic, 60 diastolic, in the left arm. The temperature was 99°F., the pulse 130, and the respirations 25.

Examination of the blood showed a red-cell count of 4,500,000 with 13 gm. hemoglobin, and a white-cell count of 16,000 with 84 per cent polymorphonuclears. The blood Hinton reaction was positive. The urine was normal. Culture of the sputum showed no beta hemolytic streptococci.

A roentgenogram of the chest showed a huge irregular cavity occupying a completely consolidated right upper lobe. The cavity was about 6 cm. in diameter, and there were multiple nodular projections along its margins. There was only a small quantity of fluid. The arch of the aorta was dilated and prominent, with a suggestion of calcification. The heart was of normal size and shape. The ascending aorta was questionably prominent. There was no definite evidence of bone destruction in the ribs or vertebrae.

The patient continued to drain large amounts of foul-smelling sputum. He was given sulfadiazine. The temperature fluctuated irregularly between 98 and 105°F. On the eighth hospital day, coarse rhonchi were audible throughout both lung fields. The patient became increasingly weaker, and cyanosis appeared. He was given gomenol, with good relief from the foul odor of the sputum. Death occurred later in the day, apparently from respiratory failure.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD D. CHURCHILL: We know that breath sounds are widely transmitted throughout the chest. I examined a man yesterday whose entire right lung had been removed three years previously; in the right axilla, there were normal breath sounds, tactile fremitus and vocal resonance. He had a thoracoplasty, but the transmission of the sounds from the left lung suggested a normal right lung in the axillary region. Pulmonary resection is giving us a new concept about

transmission of sounds into the area over which one is listening with a stethoscope. The x-ray film in the case under discussion makes it obvious that the underlying lung could not produce normal breath sounds. They must have been coming through from adjacent segments of lung.

"There was early clubbing of the fingers." I do not like the term "early." It implies that in a

vocabulary for the subtle odors so useful in clinical medicine.

The x-ray film is quite important. There is a huge irregular cavity within a homogeneously dense right upper lobe (Fig. 1). The X-ray Department are overstepping when they refer to a "consolidated" right upper lobe if they imply consolidation in the pathologic sense. The cavity is



FIGURE 1.

few months it will increase. We have no evidence for that. Some diseases give slight clubbing, others extreme clubbing, and others no clubbing of the fingers. The term "early" means slight or moderate.

I often wish we had a more ample terminology to describe the odor of the sputum because so often the diagnosis can be made by this means alone. Varying odors of the sputum are like the bouquets of vintage wines. The word "foul" does not mean anything and, in addition, always startles the patient. It may be more informative to ask if the sputum has a bad taste. The patient will tell you that his sputum tastes bad, but if you ask if it is "foul," he will say no. It is unfortunate that we are lacking a precise descriptive

6 cm. in diameter. There are multiple nodular projections along its margins.

Will you comment on the x-ray film, Dr. Schatzki? Do you care to make a more clearly definitive statement regarding calcification and prominence of the ascending aorta?

DR. RICHARD SCHATZKI: There is definite calcification in the arch of the aorta. I should say that the ascending aorta is dilated, and also the arch. The descending is normal in size so far as I can see on the film.

DR. CHURCHILL: Is the heart of normal size?

DR. SCHATZKI: Yes.

DR. CHURCHILL: Is there anything to add to the description of the cavity?

DR. SCHATZKI: I think it is a fairly good description. You are right in considering the term "consolidation" a poor one. It is very often erroneously used in the sense of density, as you know.

DR. CHURCHILL: Let us take up the question of cardiovascular disease. There was a positive blood Hinton reaction, a dilated aorta, with calcification in its walls, a rough systolic murmur over the aortic area and a blood pressure of 110 systolic, 55 diastolic.

Dr. Breed, do you want to pick that up from the medical standpoint and tell us what was wrong with the cardiovascular system?

DR. WILLIAM B. BREED: I do not believe that the variation of blood pressure between the right and left arms was more than normal. The mere recording of such figures tends to call more attention to the variation than is justified. The pulse pressure of 50 to 55 without an aortic diastolic murmur is not particularly significant, and in the x-ray picture the possibility of syphilitic aortitis is not so likely as an arteriosclerotic aorta in a man of sixty. However, I should like to question Dr. Schatzki a little more specifically on that point — can one differentiate by this x-ray film a syphilitic from an arteriosclerotic process?

DR. SCHATZKI: You mean so far as tortuosity and dilatation of the aorta are concerned. In a large number of cases of syphilitic aortitis, we call the aorta normal, knowing that we cannot see significant pathologic changes in many of them. We usually make an understatement rather than an overstatement in that respect — it is better not to call the aorta dilated than the other way around. But when we say dilatation, I think it is quite dilated, and this particular aorta was dilated in that sense. There is not such a degree of dilatation in arteriosclerosis unless there is a dissecting arteriosclerotic aneurysm.

DR. BREED: You never speak of a tortuous aorta as dilated?

DR. SCHATZKI: We should not per se. I think that is a definite mistake.

DR. CHURCHILL: Do you say that this was syphilitic aortitis?

DR. TRACY B. MALLORY: How about the calcification?

DR. SCHATZKI: I should say that syphilitic aortitis with dilatation shows calcification in a very large percentage of cases. As a matter of fact, the presence of calcification rather proves than disproves the diagnosis, particularly if the calcification is in the ascending aorta.

DR. CHURCHILL: Do you agree with that, Dr. Mallory?

DR. MALLORY: I agree with Dr. Schatzki that calcification in the thoracic aorta is unusual in the arteriosclerotic aorta except in advanced cases; in the abdominal aorta, it is a different proposition.

DR. SCHATZKI: I cannot see calcification in the ascending aorta. We often see calcification in the arch of an arteriosclerotic aorta, just where we see it in this particular case. If it were in the ascending aorta, it would be more in favor of syphilis.

DR. MALLORY: I should have qualified my statement. Calcification is common in the arch. A favorite spot is the dimple of the ductus arteriosus. In the ascending and frankly descending portions, I do not believe we often see it.

DR. SCHATZKI: We do in very advanced cases.

DR. CHURCHILL: Dr. Breed, you are still my medical consultant. What do you call this?

DR. SCHATZKI: If the patient had no definite evidence of regurgitation, I do not see how we can decide the question. Is that right?

DR. BREED: Yes; he had no diastolic murmur. This does not rule out syphilitic aortitis, but it is evidence against it.

DR. SCHATZKI: The fact that the heart shadow was normal probably rules out aortic regurgitation.

DR. BREED: Yes, probably.

DR. FULLER ALBRIGHT: Was the aortic second sound recorded?

DR. MALLORY: There is no note on that.

DR. CHURCHILL: Then you interpret this, Dr. Breed, as syphilitic aortitis?

DR. BREED: I shall take the arteriosclerotic side, for the sake of argument.

DR. SCHATZKI: I shall take the syphilitic side.

DR. CHURCHILL: We know that the patient had a pulmonary abscess, with a fluid level in a cavity and foul sputum. The only question is, Was this abscess in the center of a cancer, or was it not? We have no direct evidence for cancer other than the x-ray film and the course of the patient, which, however, is perfectly consistent with a noncancerous lung abscess. The history and physical examination do not point either way. The question whether or not this was an abscess within a cancer comes down solely, it seems to me, to interpretation of the film. I maintain that the thickened wall, with the nodule extending into the cavity, indicates that it was a necrotic tumor — a primary cancer. I can come to no other diagnosis. That is an x-ray diagnosis, and I should like to check it with Dr. Schatzki.

DR. SCHATZKI: You must remember the cases in which we used the same reasoning and were wrong! In those cases, a markedly irregular out-

line of the inside of the cavity turned out to be caused by debris in an abscess.

Dr. CHURCHILL: I do. The debris abscess gives a thumbnail appearance, rather than the picture presented by this case.

Dr. SCHATZKI: I agree; and from this film I should not hesitate to call it cancer.

Dr. CHURCHILL: I can reach no other conclusion on the evidence. The clinical course could go with either. So that, purely on the x-ray visualization of the lesion, I say lung abscess within a primary cancer of the lung.

Dr. CHURCHILL: I can mention it.

Dr. COPE: And would you exclude it?

Dr. CHURCHILL: Not definitely. I can mention it as one of the things that turn up now and then when we are wrong. It is like the safeguard of the medical student who always puts syphilis down at the end of a list to include everything in his differential diagnosis; it might be syphilis.

CLINICAL DIAGNOSES

Carcinoma of lung, with secondary abscess.

Syphilitic aortic aneurysm.

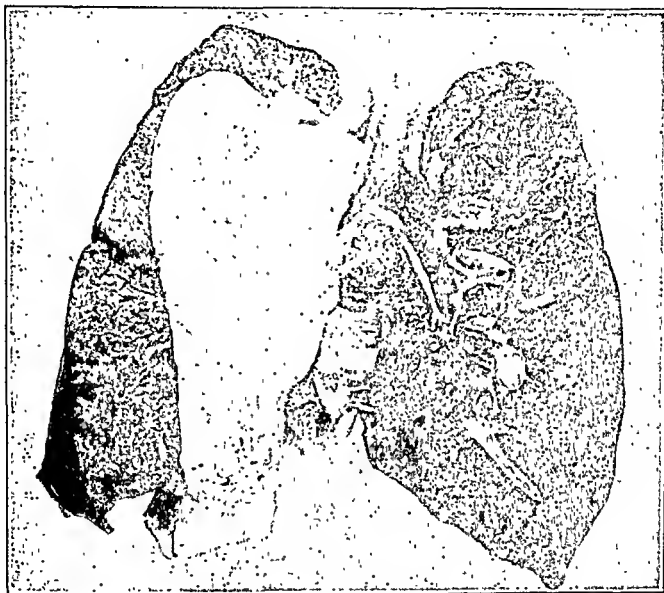


FIGURE 2

Dr. MALLORY: Do you accept Dr. Breed's or Dr. Schatzki's opinion regarding the aorta?

Dr. CHURCHILL: I have no competence to decide between them. I shall let the two gentlemen argue it out.

Dr. BREED: Dr. Albright suggests that if this was cancer in the right upper lobe, it may have pushed the aorta over to make it appear larger than it was. I think that is a good point.

Dr. SCHATZKI: I think we can differentiate between tortuous aorta and dilated aorta if it is markedly dilated.

Dr. MALLORY: Would anyone care to defend a primary aneurysm occluding a bronchus by external pressure and secondary abscess of the lung?

Dr. CHURCHILL: I am not willing to accept this as aneurysmal phthisis.

Dr. OLIVER COPE: Would Dr. Churchill mention gumma with abscess?

Dr. CHURCHILL'S DIAGNOSES

Carcinoma of lung, with secondary abscess.

Cardiovascular disease involving aorta, nature undetermined by medical and radiologic consultants.

ANATOMICAL DIAGNOSES

Carcinoma of upper-lobe bronchus of right lung, with secondary abscess.

Metastasis to regional lymph nodes and left adrenal gland.

Syphilitic aortitis with aneurysm.

Bronchopneumonia, terminal.

Urolithiasis medicamentosa (sulfadiazine).

PATHOLOGICAL DISCUSSION

Dr. MALLORY: Autopsy showed a mediastinum filled with a large aneurysm, syphilitic in origin. It replaced the arch, half the ascending and al-

most two thirds of the descending aorta, stopping sharply at a point about 4 cm. above the diaphragm. Figure 2 shows the thoracic organs viewed from behind. The dilated descending aorta has been reflected over the left lung. The cavity in the right upper lobe appears black, and a white tumor nodule is visible in the bronchus to the upper lobe. Smaller tumor masses surround the cavity. The syphilitic aneurysm was apparently coincidental and had nothing to do with the symptoms.

DR. BREED: Then it is merely an academic discussion of x-ray diagnosis. The disease had nothing whatever to do with the patient's health or death.

DR. MALLORY: So far as this cardiovascular syphilis is concerned?

DR. BREED: Yes.

DR. MALLORY: That is true.

There were metastases to the adrenal glands. These were the only distant metastases found.

DR. CHURCHILL: Was it an epidermoid carcinoma?

DR. MALLORY: It was so undifferentiated that we did not classify it.

DR. SCHATZKI: Where did the dilatation start?

DR. MALLORY: It began shortly above the valve, 1.5 cm. to be exact, but was only slight, measuring 8 cm. in circumference up to the arch; then it widened to 10 and 14 cm. farther on.

CASE 28272

PRESENTATION OF CASE

A thirty-nine-year-old housewife entered the dental clinic of the hospital complaining of a growth of tissue on her gum.

The patient had always been negligent of her teeth, occasionally pulled the loose ones herself, and eighteen years before admission had had fifteen teeth extracted. Seven years before admission, she noticed in the left upper jaw a painless growth of tissue that occasionally bled and gradually increased in size, but had remained the same for the previous three years. She had had no dental care in seven years. Examination showed a large mass of hypertrophied tissue about 3 cm. in diameter overlying the maxilla in the left cuspid area. It was firm, attached by a very hard pedicle, and had a fissure running through it in the antero-posterior direction. A tentative diagnosis of epulis was made, and the patient was referred to the medical service for blood calcium and phosphorus studies.

On the medical service, it was learned that four years before admission the patient slipped and fell,

fracturing her scapula and right patella. While in bed, she gained about 70 pounds in weight. The bones healed readily, although the patella remained displaced. Two years before entry, the patient was sick for one month with low-back pain, fever and chills unaccompanied by frequency, dysuria, hematuria or changes in the appearance of her urine. Eight months before entry, she noticed in the left neck a constant soreness, which radiated to the head and seemed worse immediately before the menstrual periods; she attributed this pain to the growth in her mouth. Dizziness and vomiting without nausea appeared five weeks before entry. The vomitus was green and watery, had no relation to meals, and occurred approximately every other morning. These symptoms were accompanied by a great thirst and craving for sour fluids. In general, the appetite was small, and the patient rarely ate sweets, milk, bread or cheese.

The patient had had the usual childhood diseases and, thirteen years before admission, a cholecystectomy and appendectomy. Her father had died at fifty of hemophilia, and her mother at fifty of diabetes. One sibling died at twenty-five of tuberculosis. She stated that her sister's children and her own two offspring might have hemophilia.

On examination, the patient was well developed and extremely obese, but appeared well. The skin was clear and of fine texture, and there was a large scar in the left breast. On the dorsum of the third left metacarpal bone was a hard tumor measuring 3 by 5 cm. There were marked pyorrhea and caries of the remaining teeth, and in the maxillary left cuspid area there was the lesion observed in the dental clinic. Examination of the heart, lungs and abdomen was negative. The right patella was displaced upward above the knee joint. Examination of the fundi and nervous system was negative.

The blood pressure was 140 systolic, 95 diastolic. The temperature was 98 to 100°F., the pulse 90, and the respirations 20.

Examination of the urine showed a +++ test for albumin, an occasional hyaline cast, and a +++ Sulkowitch test for urinary calcium. A urinary-concentration test was normal, and a phenolsulfonephthalein test yielded 18 per cent of the dye in fifteen minutes and another 10 per cent in thirty minutes. Examination of the blood showed a red-cell count of 4,190,000 with a hemoglobin of 82 per cent, and a white-cell count of 7500 with 54 per cent polymorphonuclears. The serum calcium ranged from 13.8 to 16.6 mg. per 100 cc., the phosphorus from 0.92 to 2.3 mg. per 100 cc., and the phosphatase from 3.3 to 9.7 Bodansky units. The nonprotein nitrogen of the blood serum was 17 mg. and the proteins 6.8 gm. per 100 cc. A blood

Hinton reaction was negative. The stools were guaiac negative.

X-ray films of the teeth showed absent lamina dura, with marked alveolar absorption about many, and severe caries. There was a cyst involving the alveolar process of the left upper jaw in the incisor, cuspid and bicuspid areas. The bones of the vault had a mottled appearance because of multiple small areas of rarefaction. The bones of the skeleton were decalcified. There was a large cyst involving the proximal phalanx of the left middle finger, another involving and expanding the third right metacarpal and a smaller cyst in the first right metacarpal; a fourth was present in the carpal scaphoid on the left. There was an old fracture of the left patella, with dehiscence of the fragments, and a supranumerous high epicondyle in the left humerus. X-ray films of the chest showed enlargement of the heart in the region of the left ventricle and a tortuous aorta. No pathologic mass was seen in the upper mediastinum. The diaphragm was slightly high, but there was no evidence of intrapulmonary disease. The esophagus was demonstrated by barium and was normal.

An electrocardiographic recording showed a normal rhythm, a rate of 84 and a PR interval of 0.15 second. There was slight left axis deviation, sagging ST interval in Leads 1 and 2, slight inversion of T_3 and diphasic T_4 .

One month after admission, an exploration of the neck for parathyroid tumor was performed. Both upper parathyroid glands were identified and appeared normal. No others were found.

DIFFERENTIAL DIAGNOSIS

DR JACOB LERMAN: I should like to comment on several points in the history and physical examination. The presenting symptom was that of a painless lesion of the left upper jaw, slowly growing and obviously not very malignant. The next significant feature was the story of fractures resulting from slight trauma. This immediately suggests pathologic fractures; good healing is consistent with some types of pathologic fractures. The gain of 70 pounds in weight does not seem to be significant; the low back pain, fever and chills are difficult to explain. The evidence is against urinary infection. The soreness in the left neck is also difficult to explain. If it was due to a lesion similar to the one in the jaw, the exacerbation before menstrual flow is understandable. The change in electrolyte balance that occurred premenstrually may have increased the volume of an encapsulated or enclosed mass so as to produce increased pressure. The dizziness and vomiting appeared to be nonspecific in origin. The abdominal operation raises the possibility of adhesions as a cause for

vomiting. However, the absence of pain is against this. The thirst and craving for fluids may have been caused by vomiting, by excessive excretion of sugar or electrolytes, or by symptoms of diabetes insipidus. The low intake of milk and cheese is significant.

Physical examination gives us the information of a tumor of the left hand, in addition to the one in the jaw. I cannot tell whether this tumor was part of the bone or merely adherent to it.

The important laboratory data consist of a high blood calcium, low blood phosphorus, +++ Sulzowitch test and normal to slight elevation of phosphatase. There was evidence of slight renal impairment — namely, a +++ test for albumin and occasional hyaline casts. The tests for renal function were negative. The serum protein was normal. The significant findings by x-ray were the absent lamina dura, cysts in the jaw and hand, areas of rarefaction in the vault, decalcified skeleton and old fracture of patella. The electrocardiographic changes, in the absence of digitalis, suggest coronary disease in the menopause. I cannot see why hypercalcemia should produce these electrocardiographic changes. One would rather expect changes in conduction as a result of high blood calcium.

The most logical diagnosis is primary hyperparathyroidism. The evidence for this consists in the probable pathologic fractures, dizziness, vomiting, thirst, bone cysts, bone decalcification in the presence of a low calcium intake, changes in the teeth by x-ray, hypercalcemia, low blood phosphorus and hypercalciuria. The slight renal damage is of the type seen in this disease. The relatively low phosphatase is somewhat unusual.

Several other conditions must be considered. One is secondary hyperparathyroidism; there was not enough renal damage to cause retention of phosphorus. Metastatic bone lesions, lymphoma involving bones and sarcoid are others. Any of these conditions may give a high calcium in the blood and urine, but the phosphorus is either normal or elevated. The duration of the condition and appearance of the skull in the case under discussion are against malignant lesions. Multiple myeloma is suggested by the skull plates, high blood calcium, albuminuria, low blood phosphorus, absence of Bence-Jones proteins in the urine, normal serum protein and bone cysts. If renal damage is produced by multiple myeloma, one may get the secondary type of hyperparathyroidism. Rapid mobilization of calcium results from immobilizing the greater portion of the skeleton, the blood stream being flooded with calcium and phosphorus; there is nothing to suggest the situation in this case.

Dr. Albright and I have followed 2 patients in this hospital and Dr. John Howard has followed 1 at Johns Hopkins Hospital with the following characteristics: high blood calcium and phosphorus, high urinary calcium, advanced renal damage, elevated serum protein, no Bence-Jones protein and negative sternal biopsies. The only common finding in all these cases was a history of excessive intake of calcium and alkali. This patient does not belong to this group because the renal damage was not extensive, the serum protein was normal, the phosphorus was low and the intake of calcium was low.

In conclusion, I must say that hyperparathyroidism, due either to generalized hyperplasia of all the parathyroids or to an adenoma of one parathyroid, is the most probable diagnosis. Since the surgeon did not confirm this, there are certain possible explanations. The surgeon may have been mistaken about the character of the parathyroid glands, and the pathologist may have discovered either hyperplasia or a small adenoma. The patient may have died, and the pathologist may have discovered the true nature of the disease. Knowing the perseverance of the surgeons, I suspect that a second search was made, and, as often happens, a parathyroid adenoma was found elsewhere.

CLINICAL DIAGNOSES

Hyperparathyroidism.

Parathyroid adenoma of mediastinum.

DR. LERMAN'S DIAGNOSES

Hyperparathyroidism.

Parathyroid adenoma of mediastinum.

ANATOMICAL DIAGNOSES

Hyperparathyroidism.

Parathyroid adenoma of mediastinum.

PATHOLOGICAL DISCUSSION

DR. OLIVER COPE: Dr. Lerman's surmise is correct; a second operation was performed in search of a parathyroid tumor. I have brought along a colored motion picture to show you as proof. Such pictures are expensive to make, and I should not have had this one taken of the operation if we had not been reasonably sure of the diagnosis of hyperparathyroidism.

It is fair to say that Dr. Lerman was not given all the evidence that is now available, or should be available, to the surgeon trained in the care of this disease. The two parathyroid glands disclosed at the first operation in the neck were not normal. They were atrophic, and should have been termed "uninvolved." In the presence of an adenoma, the uninvolved glands are not called on to function and undergo an atrophy of disuse. This

atrophy apparently affects only the epithelial cells, and the proportion of fat therefore rises and the color changes more to that of normal fat. It is only recently that I have been able to recognize this difference in gross appearance between the normal and uninvolved glands. This has come only by comparing the normal glands seen in patients with thyroid disease and those of patients explored in search of a parathyroid tumor who turn out not to have one with the uninvolved glands seen in patients proved to have hyperparathyroidism due to an adenoma. Microscopically, this atrophy is difficult to identify, since normally there is a considerable variation in the proportion of fat to epithelial cells; in gross at the operating table, however, the finding of a small, yellower than normal parathyroid gland does suggest the presence of an adenoma in one of the other parathyroid glands.

Having searched the neck and the posterior mediastinum at the first stage in this patient, I left the operation reasonably sure that a tumor existed in the anterior mediastinum. The presence of an adenoma had been excluded in all other possible positions in which parathyroid glands can occur. The anterior mediastinum, alone, remained. The motion picture is therefore of the exploration of the anterior mediastinum. The first step in the exploration is to expose the anterior surface of the sternum. An opening is made along the sternum in the right third interspace by insertion of a finger. The pleura is depressed and then pushed laterally. Another finger is inserted above in the manubrial notch. These are brought together beneath the sternum, and a free passage is made for the sternal knife. The pleura and pericardium are then carefully separated further by blunt dissection as the two portions of the sternum are retracted laterally. The anterior fascia within the anterior mediastinum is then opened into. At this point, we spied an adenoma lying anterior to the ascending aorta, slightly on the right side. One can see, on the far side of the incision, the pleura of the left side. The adenoma now appears in the center. It is quite a large flat tumor, and at its upper pole there are no blood vessels. As the tumor is lifted into the field, the entire vascular pedicle is at its lower pole. The arterial branches come from the mediastinal vessels feeding the upper pericardium. The position of the vascular tree is an important point. Several articles in the literature suggest that if a parathyroid adenoma exists in the mediastinum, a vascular pedicle will be found leading from the thyroid gland down into the chest. This may be true if the parathyroid gland, at the end of embryologic development, resides somewhere near the thyroid and is displaced into the mediastinum later, when it is enlarged by

the adenoma. Such displacement occurs partly by the motion of the larynx and thyroid region with swallowing, and partly by the negative intrathoracic pressure. But in this patient we believe that the parathyroid tissue arrived in the anterior mediastinum during its embryologic development. It came down with the thymus from the upper or third branchial cleft, and it derived its blood supply from the neighborhood in which it finally resided. When the adenoma developed in this gland, the blood supply, of course, remained the same. The absence of a vascular pedicle from the neck to the mediastinum therefore does not exclude the presence of a parathyroid gland in the chest. It is conceivable that one could have reached the tumor in this case from the neck incision by inserting the fingers down behind the sternum and catching it. In view of the size of the arterial blood supply, any attempt to deliver the tumor from the mediastinum into the neck would have been risky. Undoubtedly, the vascular pedicle would have torn, and there would have been an intrathoracic hemorrhage, which could not have been controlled from the neck. We have delivered three such tumors from the mediastinum into the neck, but we now know it to be risky, not only because of hemorrhage but also because of possible pneumothorax. Moreover, it is not possible to reach far enough down with the fingers inserted in the neck. One patient who came to autopsy had a parathyroid adenoma resting on the right auricle on the upper folds of the pericardium. This was at least 5 cm. below the reach of fingers inserted into the notch of the manubrium. Therefore, the operation of exploration for a parathyroid tumor is now divided into two stages. In the first stage, the neck and posterosuperior mediastinum are explored — that is, the region that can be exposed to direct vision. If the adenoma is not found in this exploration, it

must be in the anterior mediastinum. At the second stage, the sternum is split so that the anterior mediastinum can be explored under direct vision.

DR. TRACY B. MALLORY: I have only to add that the tumor was a characteristic parathyroid adenoma on microscopic section — a large one, with many glandular and cystic spaces in it.

DR. JOSEPH C. AUB: Did you look for the fourth gland?

DR. COPE: We did not. The size of this adenoma was adequate to account for the severity of the disease that this patient had. If we had found a small adenoma, we certainly would have looked for the fourth gland to make sure that it did not contain a second adenoma. About 10 per cent of our patients with adenomas have had two adenomas. The weight of adenomatous tissue is roughly proportionate to the degree of elevation of the blood calcium. This patient's tumor was a large one. The chances were against her having a second adenoma. Actually, I did look throughout the thymus gland, which was the most likely place to find the fourth, but did not encounter it. The subsequent course of the patient has shown that there is presumably no further hyperactive tissue.

A PHYSICIAN: What percentage of glands are found in the mediastinum?

DR. COPE: Of the 67 cases of proved hyperparathyroidism at this hospital, 60 were due to adenoma and 7 to hyperplasia. Of the cases with adenoma, 13 adenomas were found in the anterior mediastinum, and 5 in the posterior mediastinum. This gives an exaggerated percentage, since cases sent to this hospital for secondary explorations have turned out in large proportion to have the adenoma within the mediastinum. I believe about 10 per cent would be the true figure.

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WAR AND MASSACHUSETTS PHYSICIANS

THIS issue of the *Journal* contains a series of six papers presented at the annual meeting of the Massachusetts Medical Society that discuss the war effort as it relates to various aspects of medicine. The medical profession of any nation plays such a significant role in modern warfare—in combat areas, in training centers, in industry and in civilian communities—that each article should be carefully read by all physicians, particularly those who practice in Massachusetts, and even including those who listened to the papers at the annual meeting.

Dr. Frank H. Lahey forcefully emphasizes the need for young physicians in the armed forces,

states that *all* physicians will eventually be utilized in one capacity or another if the war continues, and exhorts those who are classified as "available" to apply immediately for commissions.

Dr. Reginald Fitz discusses the problems and experience of the Massachusetts committee of the Procurement and Assignment Service. He, too, stresses the need for young physicians and presents an analysis of the status of the 3000 Massachusetts physicians under forty-two years of age. According to his figures, 1200 of these young physicians are necessary to the health and welfare of civilians, whereas the remaining 1800 comprise a pool in which the essentiality or availability of each individual must be determined.

Dr. Elliott C. Cutler outlines the organization and modus operandi of the Medical Division of the Massachusetts Committee on Public Safety, pays due tribute to the time and effort given by Massachusetts physicians to the establishment of local medical committees, to the training of mobile medical units, to the proper equipping of hospitals and to provisions for medical and civilian evacuation, and asks that this interest be continued.

Dr. A. William Reggio covers the physician's role in first aid, particularly emphasizing the need for all physicians to become thoroughly familiar with accepted first-aid procedures, so that they may be qualified to give first-aid courses, to instruct intelligently the members of first-aid parties and the helpers of the medical first-aid posts and to apply first-aid measures themselves, if necessary.

Dr. Bennett F. Avery presents the problems that have been raised by the accelerated schedule of education adopted by nearly 90 per cent of the medical schools in this country and by the need for more detailed instruction in matters pertaining to military medicine.

Finally, Dr. Charles F. Wilinsky gives certain objectives that may be considered the minimum goal of all hospitals during the emergency. These include the protection of physical property, the care of casualties and facilities for evacuation.

All these matters are of vital interest to Mas-

sachusetts physicians, and by the publication of these six papers in a single issue of the *Journal* it is hoped that a means will be furnished whereby each physician will become thoroughly familiar with his responsibilities during the present crisis

THE SINISTER SHEPHERD

PROFESSOR SIMUEL E. MORISON* in his *Admiral of The Ocean Sea* has analyzed the available data and opinions regarding the possible transmission of syphilis from the New to the Old World as the result of the discovery of America by Columbus. One chapter, entitled "The Sinister Shepherd," is an excellent summary of all that is known of importance about this controversial subject. He should receive wide recognition from physicians for his handling of the perplexing problem, since he, a nonmedical historian, has done a better job than any medical writer on the topic.

As Professor Morison points out, the evidence appears to be sound that syphilis existed in America before the first voyage of Columbus in 1492. It was present, in all probability, among the Indians of the islands and continent. He reached this conclusion only after careful deliberation, and in spite of the fact that some historians and archeologists do not agree.

The question whether syphilis existed in Europe before Columbus returned in 1493 is a much more difficult one to answer. Everyone knows that, in 1495 or 1496, syphilis became rampant in Europe. Before 1495, however, there is no clear clinical description of a case that one can say with certainty was syphilitic. On the other hand, Sudhoff collected a great amount of evidence to prove that syphilis existed in France, Germany and Italy long before 1493. According to this eminent historian, the march of the French army on Naples in 1495 simply stirred up and spread the organism, which was already in existence. Other historians believe that Sudhoff is wrong about this matter, for he based his arguments on

uncertain data and a few clinical descriptions that may point to another disease. It seems certain, moreover, that syphilis, in the form and to the extent in which it ravaged Europe in 1495 and after, could not have been evident before that date. If syphilis had been present before that time, it must have been in a dormant form and something must have served as an activator. Was this activator the syphilis brought over by the sailors with Columbus?

Professor Morison does not believe that the sailors were actually responsible for bringing over the syphilis, but he does think that the Indian captives whom Columbus brought back on his first voyage were probably carrying the *Treponema pallidum*. None of the crew were ill, even when they reached Spain. If they had acquired syphilis before leaving the New World, they would surely have shown evidence of the disease at that time, particularly in view of the virulent type of syphilis that subsequently developed. The Indian captives, on the other hand, might have carried the disease without manifesting marked signs while on the voyage, only to transmit it to European soil where, because no one was protected against this type of syphilis, a virulent outbreak occurred. This is the basis of Professor Morison's argument, and he has presented so strong a case that it will be accepted by many. This hypothesis, moreover, is supported by three reputable writers of the middle sixteenth century—Las Casas, Oviedo and Diaz de Isla, the last a house physician in a Lisbon hospital. It seems, therefore, that America was the original home of the "sinister shepherd."

MEDICAL EPONYM

PLAUT-VINCENT'S ANGINA

Hugo Carl Plaut (1858-1928) of Leipzig published his "Studien zur bakteriellen Diagnostik der Diphtherie und der Anginen [Studies in the Bacterial Diagnosis of Diphtheria and the Anginas]" in the *Deutsche medizinische Wochenschrift* (20:920-923, 1894). A portion of the translation follows:

Five successive cases of simple angina deserve mention because of the type of micro-organism that, there seems to be no doubt, was their cause. Inspec

*Morison, S. E. *Admiral of the Ocean Sea: A Life of Christopher Columbus*. 2 vol. 893 pp. Boston: Little Brown and Company, 1942.

tion of the oral cavity, which contained many carious teeth, showed a dirty exudate on both medial surfaces of the markedly swollen tonsils and the left side of the uvula. . . . Microscopic examination of the exudate showed it to consist bacteriologically of nothing but Miller's spirochetes and Miller's bacilli. . . . Miller's bacilli are . . . much larger than the diphtheria bacilli, are, in contradistinction to these, pointed at the ends, and are always associated with the spirochetes, which apparently have some genetic relation with them. . . . These micro-organisms of Miller's are found in small numbers in almost every normal mouth, but usually only under the gum margins. [The organisms referred to were described by W. D. Miller, an American physician and dentist in Berlin, in 1883.]

H. Vincent (1862), military surgeon and bacteriologist, wrote "Sur une forme particulière d'angine diphtéroïde (angine à bacilles fusiformes) [On a Peculiar Form of Diphtheroid Angina (Angina with Fusiform Bacilli)]" in the *Bulletins et mémoires de la société médicale des hôpitaux de Paris* (15, 3rd series: 244-250, 1898). A portion of the translation follows:

This angina is characterized by a grayish or whitish pseudo-membranous exudate, by the associated fever and occasionally rather marked adenitis. . . .

If a bit of the pulpy exudate that appears on the surface of the pharynx is removed and stained with thionin or Ziehl's dilute fuchsin, microscopic examination shows two kinds of microbes to be predominant: a peculiar bacillus, easily recognizable by its length (about 10 to 12 microns) and its bulging central portion and distinctly tapering ends, and a delicate spirillum, more difficult to stain. This spirillum is quite similar to that normally present in the saliva and dental tartar.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY: FATAL PRENATAL SEPARATION OF THE PLACENTA

A thirty-seven-year-old gravida VI began to bleed when she was eight months pregnant, and was seen by her physician. The bleeding was painless; she was not in labor. No steps were taken until additional bleeding occurred, and she was sent to a hospital. In this institution, nothing whatsoever was done for her, and she was finally sent to another hospital, where she arrived nine and a half hours after the initial bleeding. On admission, the hemorrhage was brisk, the blood pressure was 72 systolic, 60 diastolic, and no fetal heart could be heard. A diagnosis of separated placenta was made. Vaginal examination revealed the cervix to be dilated sufficiently to admit one finger. The vagina and cervix were packed with gauze, and a Spanish windlass was applied. Intravenous

glucose was administered, but the patient was given no blood transfusion because no donor could be obtained. She died undelivered eight hours after entry to the second institution.

Comment. There is no information concerning the past history of this patient, and whether or not she had any prenatal care is unknown. Since there is no record of the blood pressure when she was first seen at home at the onset of bleeding and no statement of any urinalysis, it is not known whether the separation was associated with hypertension and albuminuria. The treatment accorded the patient by the physician who first saw her and by the hospital to which she was first sent is disgraceful: no examination was made, and she was not hospitalized until a second hemorrhage occurred. Her stay in the first hospital was merely a loss of time. Apparently, this institution was equipped neither professionally nor mechanically to deal with obstetric emergencies; the patient was untreated for at least two hours, and was then transferred to the second hospital. The treatment from then on cannot in any way be criticized, except for the fact that no transfusion was given. Patients with separated placenta who have a blood pressure of 72 systolic, 60 diastolic, and who have been bleeding for nine hours and continue to do so are very poor risks for laparotomy. The conservative treatment of packing the cervix and vagina and applying a Spanish windlass would in all probability have been successful had it been administered when the patient entered the first hospital.

The presence of plasma in most institutions helps materially in reducing the fatalities from hemorrhage when it is impossible to secure a blood donor.

DEATHS

LA MARCHE — WALTER J. LA MARCHE, M.D., of Cambridge, died May 30. He was in his eighty-first year.

Born in Belmont, Dr. La Marche received his degree from Laval University Medical Faculty, Montreal, and did postgraduate study in France. He was a former member of the Orthopedic Department, Massachusetts General Hospital, and of the staff of the Holy Ghost Hospital for Incurables, Cambridge. He had practiced in Massachusetts for over fifty years, and was a retired member of the Massachusetts Medical Society and the American Medical Association.

His widow, three sons and a granddaughter survive him.

SHULTIS — FREDERICK C. SHULTIS, M.D., of Leominster, died June 23. He was in his seventieth year.

Dr. Shultis received his degree from Dartmouth Medical School in 1897. He served on the staff of the Leominster Hospital. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

Two cousins survive him.

MASSACHUSETTS MEDICAL SERVICE

McCANN NAMED PRESIDENT BY BOARD

Dr. James C. McCann, of Worcester, was elected president of the Massachusetts Medical Service at the first meeting of the Board of Directors held at the Harvard Club in Boston on June 23. Serving as vice-president is Philip M. Morgan, president of the Morgan Construction Company, of Worcester. Edmund L. Twomey, attorney, of Newton, was elected treasurer. The Board meeting was the first step in a comprehensive program that will attempt to make the state-wide system for the

Massachusetts Safety Council and a member of the Executive Committee of the National Safety Council.

Mr. Twomey, treasurer, is a graduate of Holy Cross College and, in 1926, of Harvard Law School. He has practiced for many years with the Boston law firm of Palmer, Dodge, Barstow, Wilkins and Davis. He is married, has one son, and lives in Auburndale.

Pointing out that the medical profession is undertaking a radical departure from its previous mode of practice, Dr. McCann stated that the physicians are ready to accept their obligation in trying to solve the high cost of medical care accord-



DR. JAMES C. McCANN, President



MR. PHILIP M. MORGAN, Vice-President

budgeting of medical care available to the public shortly after September 1.

Dr. McCann has practiced surgery in Worcester since 1929. A native of Bangor, Maine, he graduated *magna cum laude* from Georgetown University in 1920, and from the Harvard Medical School in 1924. He received his Ph.D. in surgery at the Mayo Clinic of the University of Minnesota in 1929, and held a lieutenancy in the Army in 1918-1919. He is married and the father of six children.

Mr. Morgan, vice-president of the Massachusetts Medical Service, is a veteran of the first world war, a director of the Mechanics National Bank, of Worcester, and of the State Mutual Life Assurance Company, a trustee of Springfield College and Governor Dummer Academy, a director of the Massa-

chusetts Safety Council and a member of the Executive Committee of the National Safety Council.

ing to the American principles of democracy, at the same time maintaining the principle of private initiative and free practice.

"The launching of the Massachusetts Medical Service should lead to a very definite betterment of civilian morale," Dr. McCann said, "first, by the maintenance of health in industrial groups, and secondly, by assuring the families of the men in the armed forces that their medical-care burdens will be lightened."

Simultaneously, Dr. McCann announced that the Massachusetts Medical Society has established capital funds necessary to start the corporation in business and that Boston headquarters have been opened at 230 Congress Street. The corporation charter was granted by the State Commissioner of Insurance on May 27.

SUMMER PROGRAM

The first step in the summer program, according to Dr. McCann, is enrollment of the participating physicians. An attempt will be made for 100 per cent enrollment among the physicians remaining in civilian practice, and it is hoped that those going into the service will pledge their support.

The plan, as reported in the June 18 issue of the *Journal*, will provide budgeted payment of the full medical cost of hospital surgery, obstetrics and x-ray service for families with incomes not exceeding \$2500 yearly and for families with larger incomes on a cash indemnity basis. Later, it is proposed to extend the coverage and the benefits.

PHYSICIANS TO SERVE ON BOARD

Members of the medical profession are represented equally with laymen and subscriber representatives on the Board of Directors of the Massachusetts Medical Service.

In addition to Dr. McCann, who is serving as president, the physicians are Dr. J. Harper Blaisdell, Dr. Frank R. Ober and Dr. Samuel A. Robins, of Boston, and Dr. Charles E. Mongan, of Somerville. They have been appointed to the Central Professional Committee of the new nonprofit corporation.

Born in Providence, Dr. Blaisdell graduated from Dartmouth College in 1907 and from Harvard Medical School in 1911, and has practiced in Boston since 1914 as a dermatologist. Assistant dermatologist at the Massachusetts General Hospital for twelve years, he is now consulting dermatologist for the Winchester, Melrose, Malden, Haverhill and Exeter, New Hampshire, hospitals. He is a director of the Blue Cross and a member of the Council and the Committee on Public Relations of the Massachusetts Medical Society.

Retiring president of the Massachusetts Medical Society, Dr. Ober was born at Mt. Desert, Maine, and graduated from Tufts College Medical School in 1905. He came to Boston in 1914 as house surgeon at the Children's Hospital. Since 1937, he has been John B. and Buckminster Brown Clinical Professor of Orthopaedic Surgery at the Harvard Medical School; he is also assistant dean of graduate courses at the Harvard Medical School and professor of orthopedic surgery at the University of Vermont College of Medicine. He is surgeon-in-chief of the New England Peabody Home for Crippled Children and orthopedic surgeon at Peter Bent Brigham Hospital. He was a major in the Medical Corps, United States Army, in World War I and has been the editor or author of a number of medical volumes and papers.

Dr. Robins graduated from the Tufts College

Medical School in 1914 and did postgraduate work at the Tewksbury State Hospital and Boston City Hospital. Past president of the Greater Boston Medical Society, he is chief of the x-ray laboratories at the Beth Israel Hospital and was, for fifteen years, visiting roentgenologist of the Evangeline Booth and Boston Lying-in hospitals. He is a consulting roentgenologist to the Norwood Hospital and the Pratt Diagnostic Clinic. Clinical professor of radiology at Tufts College Medical School and instructor in radiology at Harvard Medical School, he is the author of numerous articles.

A member of the House of Delegates of the American Medical Association since 1921, Dr. Mongan received degrees of A.B. and A.M. from Boston College, and graduated from the Harvard Medical School in 1892. He did postgraduate work at the Rotunda Hospital, Dublin, and studied at Guys Hospital and the Brompton Hospital in London. Returning to Somerville as a general practitioner, Dr. Mongan has been a member of the senior staff of the Somerville Hospital since 1895 and is also a member of the staff of the Holy Ghost Hospital in Cambridge. He was the first president of the New England Obstetrical and Gynaecological Society and is a former president of the Massachusetts Medical Society. Recently, he was appointed by the Mayor of Somerville as chairman of the advisory committee studying matters concerning public welfare.

WAR ACTIVITIES

CIVILIAN DEFENSE

DECONTAMINATION SERVICES

The following letter has recently been released by the Office of Civilian Defense, Washington, D. C.:

The Office of Civilian Defense publications, *Protection Against Gas, First Aid in the Prevention and Treatment of Chemical Casualties* and *Handbook for Decontamination Squads*, outline the technics of decontamination. This letter sets forth the recommendations of the Office of Civilian Defense for the organization and administration of decontamination services.

DECONTAMINATION OF PERSONS

The decontamination of persons is the responsibility of the Emergency Medical Service. In cities within the target areas, facilities for decontamination of the wounded should be provided at or convenient to every hospital and casualty station. Facilities for the wounded should be separate from those for ambulant persons, because in a single station there will be a tendency to give priority treatment to the wounded while the ambulant become more severely burned.

It is not practicable for a city to provide complete decontamination services at the present time. Persons contaminated with liquid vesicants must be treated within five minutes to avoid severe burns; complete preparation would therefore require that facilities

be sufficiently numerous so that every individual is within five minutes walk of a decontamination station. Military authorities consider the use of gas against American cities unlikely, and the scarcity of materials precludes the possibility of extensive construction of decontamination facilities. It is desirable, however, that key personnel be trained and that plans be prepared so that facilities can be improvised and placed in operation on short notice, if necessary.

Decontamination stations should be of simple construction, with ample facilities for disrobing, bathing and chemical neutralization of agents that may have reached the skin. Wood is to be avoided in construction because it absorbs mustard gas and lewisite and is difficult to decontaminate. Brick, concrete or metal structures are preferable. All porous materials, including brick and concrete, should be painted with sodium silicate paint. Gasoline filling stations are widely distributed in most communities and offer many advantages in view of their isolation, washing facilities, and comparatively impervious construction. The Office of Civilian Defense will shortly issue plans indicating how filling stations may be adapted for this purpose.

The chief of Emergency Medical Service is responsible for organizing and training medical and other personnel to operate decontamination stations. Physicians and nurses must know how to protect themselves while handling contaminated cases, the effects of the various agents on the eyes, skin and respiratory tract, and measures for decontamination of the skin and eyes at various stages after exposure. Stations for ambulant personnel do not necessarily need a physician in attendance, but the person in charge should understand the dangers and limitations of chemical decontamination. He should also be on the alert for victims with respiratory tract, eye or severe skin exposure, who should be transferred to a hospital as soon as decontaminated. All members of emergency medical field units should be trained and drilled in decontamination.

The chief of Emergency Medical Service may appropriately request the local health department to establish and staff facilities for decontamination of uninjured persons. Public health nurses have experience in independent action and in handling groups of people, which fits them to supervise decontamination stations. Decontamination services organized and staffed by the health department for the decontamination of persons will operate as a branch of the Emergency Medical Service, under the commander of the Citizens Defense Corps.

DECONTAMINATION OF STREETS, BUILDINGS AND VEHICLES AND OF FOOD AND WATER SUPPLIES

The Office of Civilian Defense charts for the Citizens Defense Corps and the staff manual provide for decontamination squads as a part of the Emergency Public Works Service. The chief of Emergency Public Works Service has the responsibility for organization, training and administration of these squads. In their functioning their first task is rough decontamination of areas and of things in those areas. They will, in carrying out this function, use equipment, especially street flushing machines that presumably will be found in the public-works department of the usual municipality. Their first responsibility is the decontamination of streets, public buildings and the approaches thereto.

The inspection and testing for gas contamination and the decontamination of food and public water supplies are responsibilities of the municipal health department.

APPOINTMENT OF GAS OFFICERS

It is suggested that the commander of the Citizens Defense Corps appoint as a member of his staff, a senior gas officer, who will normally be chosen from the city health department. His functions will be to supply technical direction and assistance with respect to action to be taken before, during and after gas attacks. The duties of the senior gas officer are as follows:

During the period of preparation

1. He should become trained and familiar with the chemistry of war gases and the techniques and chemistry of decontamination. This information can be acquired from the Office of Civilian Defense publications and by attendance at the War Department civilian protection schools and at special schools being established by the Medical Division, Office of Civilian Defense in co-operation with the United States Public Health Service and the War Department schools.

2. He should recommend for appointment as assistant gas officers with qualifications similar to his own and train them to serve as his technical assistants to supervise decontamination of food and water.

3. He should with the chief of Emergency Medical Service select the sites for decontamination stations and provide consulting and technical service in the design and construction of these facilities.

4. He should instruct laundries in the techniques of handling various types of contaminated clothing and arrange for the safe transfer of contaminated clothing from decontamination stations to laundries and for the return of clean clothing. For this purpose, he may appoint a laundry officer from the trade in the city.

During the period of operation

1. Identification of chemical agent or agents used in an area.

2. Determination of the extent of the area contaminated, and advice to wardens and police in the vicinity concerning the type of agent or agents and the extent of contamination.

3. Inspection and technical advice concerning the decontamination of streets and buildings and reports to the police and wardens when an area is safe for movement.

4. Inspection of food and water supplies, and supervision of proper measures for their decontamination. (In dealing with food and water supplies, he should train and utilize the personnel of the municipal health department regularly employed for the supervision of food and water supplies.)

5. Collection and safe transportation to laundries of contaminated clothing and return of clean clothing to decontamination stations or hospitals (through laundry officer).

6. Inspection and technical control of decontamination of vehicles, equipment and machinery, including ambulances and other vehicles used in the transportation of casualties.

REPORT OF MEETING

NEW ENGLAND PATHOLOGICAL SOCIETY

A regular meeting of the New England Pathological Society was held on February 19 at the Massachusetts General Hospital.

Before and after the formal portion of the meeting an exhibit of pulmonary surgical specimens was demonstrated by Drs. Klopstock, Churchill and Castleman. The exhibit consisted of large watch-glass preparations, together with photographs and x-ray films of cases of bronchiectasis, lung abscess, cancer, bronchial adenoma, tuberculoma and tuberculous bronchial stenosis.

The first paper, "Subdural Abscess: A clinicopathologic study," was presented by Drs. Charles S. Kubik and Raymond D. Adams. The clinical features and pathological and surgical observations in 14 cases of subdural abscess were described. The sources of infection were paranasal sinusitis in 12 cases, otitis media in 1 case, and bronchiectasis with metastatic infection in 1 case. The symptoms in the cases in which abscess complicated sinusitis conformed to a fairly definite pattern: acute sinus infection, usually an exacerbation of chronic sinusitis; orbital swelling; pain or headache, at first localized, later becoming generalized and increasing in severity; rise in temperature, as a rule to 103°F. or higher; leukocytosis; stiffness of the neck; drowsiness, rapidly increasing to stupor and coma; and focal signs, which appeared at about the same time as drowsiness or stupor. Hemiparesis or hemiplegia occurred in every case. Paralysis of contralateral deviation of the eyes nearly always developed, and aphasia was observed in most cases of left-sided abscess. Jacksonian seizures were fairly common.

Spinal-fluid pressure, which was nearly always increased, ranged from normal to the equivalent of 350 mm. of water. Cell counts generally ranged from 150 to 600 per cubic millimeter, with polymorphonuclear leukocytes predominating, although in 1 case the count was 15 (lymphocytes) and in another 1200 (95 per cent polymorphonuclear leukocytes). The sugar content of the spinal fluid was normal. Chlorides were slightly decreased in 2 cases and normal in 12. The total protein ranged from 49 to 186 mg. per 100 cc. No organisms were found in smears or cultures.

Except for absence of sinus infection and orbital swelling, the clinical manifestations in the 2 other cases, secondary to otitis and bronchiectasis, respectively, were similar to those complicating sinusitis.

The course was rapidly progressive. In 12 cases, death occurred six to twenty days after onset of headache, and two to eight days after focal signs were first observed. In 2 cases, recovery took place after drainage of the abscess following a frontoparietal craniotomy.

In a majority of the 12 cases in which autopsy was performed, extension to the subdural space took place by direct extension through the dura; in the remainder, there was thrombophlebitis involving the venous sinuses, usually the superior longitudinal. The subdural pus in all cases covered the greater part of the lateral surfaces of the hemispheres, the greatest amount being situated over the lateral aspects of the frontal lobes. It was not encapsulated, although in some of the cases of old abscess, there was organization of the exudate on the inner surface of the dura. There was regularly a localized subarachnoid exudate,

conforming in its distribution to that of the subdural exudate, but scarcely any generalized meningitis. The frontal lobes beneath the abscesses were depressed, somewhat as with subdural hematoma, and in the underlying cortical gray matter there were severe ischemic necrosis and, in most cases, thrombosis or thrombophlebitis involving the subarachnoid veins.

It was pointed out that the clinical picture in each case was similar and that the diagnosis can therefore be made in time to save some of the patients. Drainage, it was thought, should be through a lateral frontal craniotomy opening, and not through the frontal sinus or a mastoidectomy wound. Performed in this way, the operation is simple and quick, and if the results are negative, little or no harm is done, provided that the brain is not explored. Once an empyema has developed, nothing is to be gained, and much may be lost, by operation on the sinuses or the mastoid. These may be taken care of later, if necessary, as was done in the 2 cases in which recovery took place.

The second paper, "Isolation of Pleuropneumoniae-like Organisms from Human Patients," was presented by Drs. William E. Smith and Louis Dienes. In a consecutive series of cultures from the genital tract of 129 unselected patients, pleuropneumoniae-like organisms were recovered from 23 of 77 cervical cultures, from 1 of 8 vaginal cultures, from 3 of 36 prostatic cultures and from 1 of 8 cultures of urethral discharges from men. It is apparent that these organisms are common inhabitants of the human genital tract. The question then arose whether they are saprophytes or pathogens.

The four male patients who yielded an abundant growth of these organisms all had chronic prostatitis. One had rheumatoid arthritis, 1 had polyarthritis clinically resembling gonococcal arthritis, and 1 complained of soreness of the feet and knees and swelling of the fingers. Specimens of synovial fluid were obtained from 2 of these patients, but no organisms could be demonstrated in them. Pleuropneumoniae-like organisms were recovered in only 1 other case, that of a man who also had chronic prostatitis.

Among the women, considering only those in whom pleuropneumoniae-like organisms were predominant, 5 had chronic cervicitis, 7 had gonorrhea, and in 4, the cervix appeared clean. One had a polyarthritis clinically resembling gonococcal arthritis, 1 had rheumatoid arthritis, and 3 complained of various skeletal aches and pains. Synovial fluid was obtained from the first-mentioned patient but was sterile. One of these patients was the wife of one of the male patients, a finding that suggests the possibility of transfer of the organisms by sexual intercourse.

In addition to the patients in this series, pleuropneumoniae-like organisms were obtained from any cervical cultures and specimens from purulent complications. Several of these cases presented the clinical picture of acute gonococcal cervicitis. Cultures and smears were repeatedly negative for gonococci, but pleuropneumoniae-like organisms were present in large numbers and in almost pure culture. One patient, an eighteen-year-old girl, developed an acute vaginitis with purulent discharge four days after intercourse. An abundant growth of pleuropneumoniae-like organisms was recovered from this discharge. In another case, these organisms were recovered in pure culture from an abscess of Bartholin's gland. In a case of salpingitis, pleuropneumoniae-like organisms and a few colonies of diphtheroids were cultivated from the pus expressed from the tubes. In a case of peritonitis secondary to salpingitis, an anaerobic bacillus (genus, *Bacteroides*) was obtained in pure culture from the peritoneal pus, and pleuropneumoniae-like organisms were subsequently separated from the

cultures of this bacillus as a variant growth form. This patient made an uneventful and prompt recovery from her peritonitis, pleuropneumonia-like organisms were recovered from the cervix, indicating that the cervix had been the portal of entry of the infection. Gonococci could not be demonstrated in any of these cases.

The picture that is beginning to emerge from the evidence at hand is that pleuropneumonia-like organisms, like many other bacteria, may live in the genital tract without causing any obvious disease, however, they are capable of acting as pathogenic agents either alone or in combination with other bacteria. When they cause disease, they produce a clinical picture that is similar to gonococcal infection, in that a purulent discharge develops and such complications as abscess of Bartholin's gland, salpingitis and peritonitis may ensue. In men, these organisms have been found only in cases of chronic prostatitis. One must bear in mind the possibility that these strains may represent variant forms of bacteria, as suggested by Dr Dienes in the subsequent paper.

The incidence of arthritis in this series is of particular interest because arthritis is a common complication of both the natural and the experimental diseases produced in animals by organisms of this group. Dr Smith has not been able, however, to recover pleuropneumonia-like organisms from diseased joints, although a considerable number of specimens of joint fluids, synovial tissues and subcutaneous nodules from arthritic patients were examined.

The third paper, 'The Nature of Pleuropneumonia-like Organisms,' was presented by Dr Dienes. According to the generally accepted opinion, the etiologic agent of bovine pleuropneumonia and morphologically related organisms belong to a distinct class. The organisms of this group have characteristic physical properties, morphology and mode of reproduction. They are soft and have no rigid membranes. They show an extreme pleomorphism, growing from small filter passing granules and fine filaments into large soft bodies 20 microns or more in diameter. These large bodies take part in multiplication either by germination or by breaking down into small granules. These properties make it appear that there is no similarity in any essential characteristic between the pleuropneumonia-like group of organisms and ordinary bacteria.

It was therefore very surprising when an organism of the pleuropneumonia group was found in a bacterial culture (*Streptobacillus moniliformis*). This association is so close that the bacteria cannot be freed from the pleuropneumonia-like organism. The study of this association brought forward the following facts: the organism is not present in the bacterial cultures as a contaminant or symbiont but develops by the transformation of the bacteria, the two forms are serologically similar, reacting equally well with the agglutinating serum produced against either, and for a certain period after isolation, the pleuropneumonia-like forms easily revert into the bacterial forms. These facts make it certain that the connection between the two forms is not a bacterial association but that they are variant forms of the same organism.

Dr Dienes has observed similar variants in cultures of *Bacterium funduliformis*, a flavobacterium, *Haemophilus influenzae*, *Escherichia coli* and the gonococcus. He was able to separate the pleuropneumonia-like variants of *Bact. funduliformis* and the flavobacterium and to propagate them in pure culture.

On the basis of these observations, Dr Dienes believes that the organisms of the pleuropneumonia group do not constitute a class unrelated to the bacteria but that they represent a variant growth form of bacteria. With

S. moniliformis, this variation has been shown to be reversible. The colonies of the streptobacilli can be seen to produce the pleuropneumonia-like variant, which then breeds true on repeated subculture on agar plates, but re-produces streptobacilli when placed in broth. In other cases in which pleuropneumonia-like forms were produced by organisms such as *Bact. funduliformis* and the flavobacterium, the pleuropneumonia-like forms have not been observed to revert into bacterial forms but it should be added that these strains were only recently isolated and have not been intensively studied.

The observation of pleuropneumonia-like variants in cultures of several different bacteria and, in particular, of reversible variation in well studied cultures of *S. moniliformis* makes it reasonable to hypothesize that pleuropneumonia-like strains that show no relation to bacteria represent so-called fixed species which developed as non-reversing variant forms from ordinary bacterial organisms. For example, the organisms of bovine pleuropneumonia, agalactia and human strains appear to be such fixed species.

The discovery of this new type of bacterial variation may have considerable significance. The pleuropneumonia-like organisms are filterable, they are similar in staining properties to the viruses, and the diseases that they cause have usually been mistaken for virus diseases. Their further study may explain some of the unsolved problems of infectious diseases.

In the discussion of these two papers, Dr Tracy B Mallory emphasized the point that Dr Dienes had opened up a field of great potential value but that it is too early to see how great its practical importance is, although it may prove to be considerable. Some of these cases which Dr Smith had spoken of as vaginitis or cervicitis, were cases that clinically were believed to be characteristic of gonococcal infection. Dr Mallory said that he had seen two or three cases reported to the State Department of Public Health as gonorrhea, but the most careful check, both by symptoms and repeated cultures, always failed to reveal the gonococcus. It seems quite probable that these were false reports and that the cases represented infection with one of the pleuropneumonia-like organisms.

In answer to the question how the name 'pleuropneumonia' was arrived at, Dr Dienes explained that the first organism of this group to be discovered was the etiologic agent of bovine pleuropneumonia, a very serious disease of cattle in Europe. Since then, other organisms of similar morphology have been found and have been called pleuropneumonia-like organisms.

The last paper, Renal Biopsies from Hypertensive Patients, was presented by Dr Benjamin Castleman. During the past year he has had the unique opportunity of studying the renal tissues removed at biopsy from 70 patients during the course of splanchnic sympathectomies for the relief of hypertension. More than half the patients were under forty years of age, and the average age of the group was thirty-nine years. About two thirds of the group had normal renal function as measured by the phenolsulfonphthalein test. All but 3 cases showed definite vascular disease, the severity of which was classified into four groups, Grade I being the least involved and Grade IV the most. The arterial and arteriolar lesions were of old type: intimal hyalinization, medial hypertrophy and endothelial hyperplasia. Any individual case might show lesions of only one type or of combinations of them. An attempt was made to correlate the grade of vascular disease with the renal function and with the appearance of the eyegrounds. Although in most cases the degree of

renal disease compared favorably with the degree of renal function, in a few cases there were some inconsistencies. There was not, however, so good a correlation between the renal and the retinal vascular disease. For example, a few of the normal and Grade I renal disease cases had Grade III or IV eyeground changes. Although all but 3 cases showed renal vascular disease, it was not suggested that the vascular disease must necessarily precede the hypertension, because a large proportion of patients from whom biopsies are not available but who had the same radical operation (bilateral total splanchnic resection from the semilunar ganglion to approximately the midthoracic level and resection of the sympathetic trunk from the ninth dorsal to the first or second lumbar segment, inclusive) now have normal or almost normal blood pressure. In other words, many of these patients were benefited despite their renal disease. Dr. Castleman concluded that it was quite possible that the renal disease might be secondary to the hypertension and that, if the renal changes are only slight, sympathectomy might allow for a reversible reaction. If the renal vascular disease is severe, the anatomic changes are probably irreversible, but even in these cases clinical improvement may be very striking. One case was cited in which a second biopsy specimen, removed one year after the first from a twenty-seven-year-old woman, showed that, although the blood pressure, which was 235 systolic, 145 diastolic, before splanchnic resection, was then normal, the renal disease (Grade III) had not changed.

The discussion centered about the earliest changes noted in these cases, and Dr. Castleman stated that, although it has not been definitely proved, he believes that intimal hyalinization of the arterioles, rather than medial hypertrophy, may be the first anatomic evidence of hypertension.

BOOK REVIEWS

Roentgen Interpretation. By George W. Holmes, M.D., and Howard E. Ruggles, M.D. Sixth edition, thoroughly revised. 8°, cloth, 364 pp., with 246 illustrations. Philadelphia: Lea and Febiger, 1941. \$5.00.

When a textbook on a specialized subject requires six editions in twenty-two years it usually means either that there is a great demand for the book or that the subject matter is changing rapidly. Probably both facts are true of this work. The newest edition is largely the work of the senior author, Dr. Holmes, since Dr. Ruggles died in 1939, while the revision was being made.

This edition is again a concise, accurate statement of the important facts in diagnostic roentgenology, and has been brought up to date with many additions to text and illustrations. There are no unconfirmed or unreliable statements with which one can take issue, and only the time-tested and proved methods and principles are described and illustrated. Its short concise and conservative descriptions are models of accuracy and brevity and are in themselves an index of work based on analytic reasoning.

This is an excellent up-to-date presentation in textbook form of the principles and most of the details of roentgenologic interpretation. It does not pretend to be a complete or exhaustive treatise on all phases of the subject or an encyclopedia of roentgenologic diagnosis, and yet it is surprising how well the subject is covered in so little space. If anyone could learn and retain all the information between its covers, he would indeed be well equipped

to begin the practice of this specialty — lacking perhaps only the judgment born of long experience, some of which the author imparts to his reader.

There are but a few minor criticisms, which if heeded might make a good textbook even better: all the illustrations, unfortunately, are "positives," that is, the reverse in black and white of the original x-ray films — this is quite confusing to many students who are unable mentally to transpose the shadows to their original values; the index, which is after all one of the major parts of a textbook, — the can opener, one might say, — is rather scanty and in places incomplete; more of the illustrations could be clarified by a short description pointing out the salient features of the case or illustrations selected; and even greater benefit would accrue to the reader if the simple clinical facts or symptoms or the underlying pathologic process, could be tied in more frequently with the roentgenologic findings.

The typographic errors are but few and not serious. The references at the end of each chapter are largely to important source articles that give the details to those seeking further information. The printing, binding and mechanical details are excellently carried out, and the whole book is again the most valuable brief textbook of roentgenologic interpretation in the English language.

The Essentials of Occupational Diseases. By Jewett V. Reed, M.D., and A. K. Harcourt, M.D. 8°, cloth, 225 pp., with 1 chart. Springfield, Illinois: Charles C Thomas, 1941. \$4.50.

In this day of wartime industry, all physicians should know the hazards to which the worker is exposed, especially because substitution is bound to be prevalent for necessary materials formerly obtained from foreign sources. This small volume is an excellent compendium of such information.

The symptoms, diagnosis and treatment of occupational disease are considered. The first half of the book is devoted to chemical poisons; then, physical agents are described. Various industrial dermatoses, including cancer, are discussed. Occupational diseases of the lungs and infectious diseases are briefly summarized. A very abbreviated chapter on functional disturbances associated with occupational diseases affords an interesting ending for the book. Prevention, which the reviewer considers the most important phase in any study of occupation, is unfortunately omitted.

This handy reference book should be in the library of all physicians.

Theory of Occupational Therapy: For students and nurses. By Nora A. Haworth, M.A. (Cantab.), M.R.C.S., L.R.C.P., D.P.M., and E. Mary MacDonald. With a foreword by Sir Robert Stanton Woods, M.D., F.R.C.P. 8°, cloth, 132 pp., with 81 illustrations. Baltimore: Williams and Wilkins Company, 1941. \$2.00.

This practical manual, fully illustrated, gives a detailed account of the technic of occupational therapy as practiced in mental and other hospitals in Great Britain. Although the theory is stressed, much space is also given to the apparatus, finance, storage and similar problems. Written by authors of long experience, well known in America, this book is a welcome addition to the subject. The illustrations are particularly good.

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THE RECOGNITION OF OCCUPATIONAL DERMATOSES*

C. GUY LANE, MD†

BOSTON

THE recognition of occupational dermatoses is a subject that needs review and requires some emphasis. Physicians are still too apt to think that because a person works at a certain job, any eruption he may develop is related to that job. Thus, the implication is that an eruption in a cement worker is due to cement, or that one occurring in a printer is due to turpentine. A physician is likely to be influenced by a worker who states at the first visit, "I got this rash from my job." It is also possible that, by failing to consider all the factors in a given case, a physician may deprive a worker of his just compensation or, on the other hand, permit a worker with a definite non-occupational dermatosis to receive compensation because of a wrong diagnosis.

The subject is particularly pertinent because of the present emergency. More men and women are being employed in newly created jobs. Therefore, many persons with limited training are at work on defense jobs. They may have been transferred from one job to another that uses substances which, to the workers at least, are new. They may have had some training for the job, but this training has not always concerned the dermatologic hazards, the prevention of skin injury, whether traumatic or chemical, or the care of the skin. The cry is for speed and more speed, and speed always paves the way for carelessness. The emphasis is on planes, tanks, guns and other defense items, and production is the main effort. Therefore, it can be expected that industrial accidents and diseases will increase, and with them will increase the occupational dermatoses, because 65 per cent of all industrial disease, according to figures obtainable at the present time, concern the skin. At present, in Massachusetts, approximately 300 cases of industrial dermatoses are reported each year; no doubt, an equal number or

more are not reported. In Ohio, 900 to 1000 cases a year are reported, and even in that efficient state there are undoubtedly more cases. A conservative estimate of 25,000 cases a year in this country can be made, but it is very easy to imagine that this figure will be doubled or tripled under present conditions.

If these figures are considered from the standpoint of disability, the item of "days' work lost" assumes almost alarming proportions. In Massachusetts, for one year, almost 20,000 days were lost because of occupational skin conditions. In Ohio, 39,000 days were lost in one year. Among federal employees, several years ago, 12,000 days were lost. In New York City, 40,000 days were lost in 1934. In a group of my own of 40 shoe workers whose disability was calculated, a total of over 1400 days was lost, the average being 35 and the longest 672 days. The disability from occupational dermatoses can accordingly constitute a real menace to production. Such disability may be partial or temporary, but it may be total and permanent as a result of industrial damage to the skin. It is easy to see that this menace can be as serious as sabotage or strikes in slowing up defense work, especially if trained personnel is affected. It behooves physicians, therefore, to be on the watch for such cases, and to look out for them as correctly and as justly as possible on the basis of all the facts in a given case.

One of the principal aims should be to detect these cases early, and thus to prevent the extension of the process and limit or prevent disability, not only for the good of the individual workmen but also for the sake of production in any particular factory. Early recognition also averts involvement of other workers because if a logical preventive program is carried out there will be a survey of materials and processes with which the workman is occupied, and there will be a change in the process or materials if it is possible, or at least preventive measures may be adopted before other pre-

*Read before a clinical meeting of the Maine Medical Association, Portland, October 17, 1941.

†Clinical professor of dermatology, Harvard Medical School; chief, Department of Dermatology, Massachusetts General Hospital.

sons are injured in the same way. Early detection gives an opportunity for prompt and proper treatment,—not only for the patient but also for the eradication of important causal factors. Thus, the abnormal condition will clear up more quickly, and the worker will be back on his job sooner.

A great opportunity is offered, in my opinion, to foremen, forewomen, industrial nurses and industrial physicians and surgeons, whether full or part time, to aid in this recognition of occupational dermatoses by early detection of the individual case. A similar opportunity is also offered to the general practitioner of medicine, especially in a manufacturing city. Many patients still prefer to go to their family physicians rather than to the physician or dispensary connected with their particular manufacturing plant. There are also many small shops that do not have any medical service. These foremen, nurses or physicians are all in the first line of defense against such hazards for the skin, and they should be aware of the responsibility for the early detection of *pathologic conditions of the skin for which occupational exposure can be shown to be a major, causal or contributory factor*—these words define well and briefly an occupational dermatosis.

In the dermatologic cases that fall into this group, certain significant items usually aid in the recognition of their status, both in the history and examination. Such items deserve more careful study because they point the way to the successful classification of the individual case. And such consideration of an occupational factor will be required, in all probability, in 15 to 20 per cent of all skin cases.

History

The usual procedure with any new or old case is to obtain a history of the present complaint, and in suspected occupational cases, an accurate history—not only of the existing manifestations but also of the occupation, substances handled, processes, cleansing methods and so forth—is of great value. The primary considerations, in my opinion, are questions on the duration and the site of involvement, both at the outset and subsequently. The duration has little special significance, for some cases may be acute and others chronic. But the site of the dermatosis assumes great consequence, especially if the hands or hands and arms alone are involved. If one is sure that the process is a dermatitis or eczema and not a disease such as lichen planus or erythema multiforme, it is really necessary to exclude an occupational factor as a cause, because the incidence of involvement of these sites is high in cases of dermatitis from occupational causes.

The onset and course of the disease may hold several important clues to occupational causation. The patient may observe that the beginning of the eruption was “due to his work,” but the physician should not be too greatly influenced by such a statement. In general, the site of onset is coincident with the site of maximum exposure or trauma. Furthermore, the time relation between exposure or trauma and the onset of the dermatosis should be correct for that particular dermatosis. Thus, an acute dermatitis should appear within a week after the exposure (although usually sooner), whereas a keloid may require several months, and a radiodermatitis a year or more. Another major consideration is the history of the course of the disease. If there is a story of several attacks of a similar type of dermatitis following exposure on return to a job, and remissions following layoffs, vacations or week ends, valuable evidence of an industrial causation is developed.

Somewhere in every dermatologic history, there should be a question on occupation, although the details need to be pursued only in cases that warrant it. In numerous occupations with a high degree of cutaneous hazards (Table 1), the details

TABLE 1. Occupations with High Cutaneous Hazards.

Bakers	Lithographers
Building cleaners	Machinists
Cement workers	Painters
Chemical workers	Photographers
Dishwashers	Shoe treers
Dye handlers	Soda-fountain workers
Electroplaters	Tanners
Gardeners	

should be sought. On the other hand, a truck driver may require questioning on the details of his particular job. I have emphasized the need of two histories—one of the disease and the other of the occupational factors. This is usually a time-consuming procedure but usually pays large dividends.

Of particular interest in the occupational history are the agents used. Many different agents have been described as causal factors (Table 2), and

TABLE 2. Industrial Agents Frequently Producing Skin Disturbance.

Acids	Paints
Alkalies	Petroleum products
Dust	Paints and woods
Dyes	Rubber compounds
Metals	Solvents

new substances are constantly being employed in industry. If the patient being questioned is working with substances known to have produced many cases of skin disorder, more careful consideration

should be given to the possibility of an occupational dermatosis.

Attention should be directed not only toward the agents employed in the actual process, but

TABLE 3. *Cleansing Agents Frequently Producing Skin Disturbances.*

Water	Degreasing agents
Alkalies	Naphtha, gasoline and so forth
Strong soaps	Acetone
Soda, soda ash and lvs.	Turpentine
Bleaching powders	Alcohol and its substitutes
Quick cleaners of various types	Oil
	Kerosene
	Machine oil
	Paraffin oil

also toward the substances used as cleansing agents during or after working periods (Table 3), for these are often primary or contributing causes.

Two other questions should be included if any suspicion of occupational causation is aroused. The first concerns the involvement of the skin of other workers at the same job as that of the patient being questioned. Such eruptions may be coincidental, but the matter deserves further consideration. The second question or set of questions should include possible nonoccupational contacts or trauma that might cause a skin disturbance similar to the one presented by the patient. Thus, the questions in a case of dermatitis might cover exposure to poison ivy, painting at home, cementing for a neighbor, part-time work developing photographs and so forth. Such a history casts definite doubt on the occupational process as the sole causative factor.

In any history, dermatologic or otherwise, there should be queries concerning therapy, both external and internal. Numerous drugs may produce eruptions, and occupational or other skin disease is frequently masked, altered or exaggerated by local applications. Twenty-five per cent of all dermatitis may be of therapeutic origin, and it may consequently be difficult to evaluate the original condition of the skin.

In summary, the recognition of an occupational dermatosis depends in part on the careful evaluation of certain factors obtained by questioning—the site of onset, course, time relation, details of occupation, agents handled, cleansing substances used, status of fellow workers and possible nonoccupational contacts.

Examination

In the examination of the patient, certain other factors must be weighed. In the first place, the site or sites of maximum involvement should be noted. In occupational cases, these sites coincide generally with the sites of maximum exposure to a

particular substance, and any discrepancy requires careful study.

Secondly, the types of lesions should be noted. A careful inspection should be made of the color, arrangement and so forth, together with such other general examination as is necessary to make a correct diagnosis, if possible. If a definite causal factor is suspected, the dermatosis should in general consist of lesions described in similar cases previously reported. Thus, one does not expect to find in a shoe treer the type of lesions and arrangement seen following contact with poison ivy.

Inspection should also reveal the stigmas of the patient's occupation—that is, the calluses produced by pressure and friction, the stains and pigmentation caused by materials used in his work and so forth. Such findings give additional evidence of the occupation and aid in confirmation of other findings.

At the same time, a healthy suspicion should cause the physician to be on the watch for other skin disease, nonoccupational as well as occupational. The finding of patches of psoriasis on an elbow or the presence of scars suggesting syphilis necessitates a review of other findings.

Further examination by pertinent laboratory work, biopsy, cultures, serologic tests, microscopic study of scales or pus and so forth should be carried out, if necessary.

In cases of dermatitis, patch tests with the suspected material offer a means of identifying the etiologic agent, even though the results of such tests are overemphasized at present. Numerous false-positive and false-negative reactions are reported, perhaps partly from variations in technic and interpretation. Patch tests, by themselves, should be regarded as confirmatory of the history and examination and not as diagnostic. It is necessary that they be properly performed by accepted procedure and correctly interpreted by physicians with adequate training in this field to have the proper value in the estimation of an occupational cause.

Diagnosis

After such a history and examination, the next step is the dermatologic diagnosis, without regard to the occupational factor. In other words, Is the correct diagnosis of the patient at hand dermatitis, carcinoma, lupus vulgaris or lichen planus? If the diagnosis is a disease in which there has been no previously described occupational factor to the best of one's knowledge and belief, it can be said that occupational dermatitis need not be considered. Thus, lichen planus, erythema multiforme, scabies, alopecia areata and so forth can be regarded as nonoccupational dermatoses. If the

condition is recognized as one in which previous cases have been shown to be of occupational origin, some of which are shown in Table 4, the

TABLE 4. *Diseases in Which the Question of Occupational Origin Most Frequently Arises.*

Acne	Actinomycosis
Burns	Anthrax
Calluses	Blastomycosis
Chilblains	Erysipeloid
Dermatitis, acute	Impetigo
Dermatitis, chronic	Paronychia
Eczema	Pus infections
Epithelioma	Syphilis
Folliculitis	Tinea
Keloid	Tuberculosis
Keratosis	
Radiodermatitis	
Ulcers	

decision must be made regarding the diagnosis of an occupational dermatosis and the recognition of the causal factor or factors. It is not enough to make a diagnosis of an occupational dermatosis, — acne, keloid or folliculitis, — for it is essential for the development of proper preventive measures

TABLE 5. *Causes of Industrial Dermatoses.*

Physical	Chemical
Mechanical	Oxidizing agents
Friction, pressure, traction and so forth	Reducing agents
Thermal	Infectious
Heat	Bacteria
Cold	Fungi
Actinic	Animal parasites
Sun	
X-ray and radium	

to detect the cause. These causes are manifold, and much space would be required to list them all. Their wide variation is indicated in Table 5.

In the search for causes, not only is a careful review of the history and the examination essential but much is contributed by a knowledge of previous literature on the subject. It may be necessary to inspect the process, to interview the foreman, chemist, nurse or manager, and to perform patch tests, chemical investigations and bacteriologic and pathological studies to confirm the ultimate cause. In numerous cases, it is desirable to make full use of the facilities of the Laboratory of Dermatoses Investigation of the United States Public Health Service in Washington and the Council on Industrial Health of the American Medical Association for a solution of individual problems.

Diagnostic Difficulties

In discussing this subject, I am aware of the obstacles that present themselves: the language difficulties, the intelligence and co-operation of the patient affected, or rather, the absence of them, the lack of accurate knowledge of the average employee of processes and materials, the long duration of disease before a competent opinion is

obtained, the previous and often excessive treatment, the fact that other agents may cause similar manifestations, and the apathy or possibly the dislike of some manufacturers to disclose trade formulas and other secret information.

I am also cognizant of the obstacles in diagnosis for the industrial physician or general practitioner who has had dermatologic training only in his regular medical-school course. There is enough difficulty for the trained dermatologist in many cases. General practitioners see a relatively small number of cases of the same disease, whether it is scabies, lichen planus or lupus erythematosus. It is natural, therefore, that they will not have a familiarity with the atypical and borderline manifestations, and especially the overtreated cases. Moreover, many physicians lack the knowledge of the actual ingredients that the worker is using and of the processes employed.

Furthermore, I am aware of the difficulty encountered in rendering a clear-cut opinion of occupational or nonoccupational liability in every case, for many cases must be classified as "probably" or even "possibly" industrial. In addition, in some states, only certain diseases are listed in a category legally acceptable for compensation. In other states, compensation is granted for complications of occupational dermatoses or for exaggeration by occupation of existing skin disease.

There is thus a definite need for the adoption of more uniform legislation covering this field, for a more systematic review of suspected cases, for the establishment of acceptable standards of definition, criteria and so forth, and for the development of well-standardized preventive measures that can be universally adopted. Wide publicity must be given to the fact that occupational diseases in general are preventable and that the fullest use of accepted medical procedures will definitely aid in the recognition of this group and thus prevent not only disability of the patient but also possible serious disturbance to industrial production.

SUMMARY AND CONCLUSIONS

Emphasis is placed on items in the history and examination that may aid in the recognition of occupational dermatoses.

Early detection is stressed as a most valuable aid in preventive measures.

Some of the causes and manifestations of occupational dermatoses are reviewed, and some of the difficulties in deciding these cases discussed.

The belief is expressed that a more careful consideration of this group of patients will enable physicians to recognize the occupational cases earlier and thus render better service to patients and to industry.

416 Marlborough Street

THERAPEUTIC EVALUATION OF TESTOSTERONE IN PERIPHERAL VASCULAR DISEASE*

SAMUEL B. BEASER, MD,† AND THOFDORÉ B. MASSELL, MD‡

BOSTON

THE diversity of opinion regarding the value of the numerous forms of therapy in current use for peripheral vascular disease, we believe, is due to the inadequacy of the tests of circulatory function so far utilized.

Walking is a reliable quantitative test of function if judged on the basis of capacity to walk until pain occurs. It is an easily repeated measurement of tolerance and is capable of standardization. It does not involve the use of special apparatus, and it tests muscles that the average elderly patient is accustomed to using—in other words, it constitutes a normal activity for the patients concerned.

Chronic progressive occlusion of the vascular supply to an extremity proceeds in three stages: the long preliminary period free of symptoms, except perhaps absence of pulsations in the dorsalis pedis artery; the interval of intermittent claudication, when the blood flow has been reduced by fully two thirds,¹ which continues for months or years until further substantial reduction in blood supply is obtained; and the final period, which is characterized by trophic disturbances in the skin, rubor and, eventually, skin infection.

The patient usually seeks relief in the second stage. Therapy is generally intended to promote improvement in the circulation of the muscles by vasodilating or other agents, which act presumably by encouraging an increased flow in the collateral vessels. Since the vascular supply to the skin stems from the deep (muscular) vessels, postponement of the superficial tissue breakdown that leads to gangrene and amputation may be achieved.

Measurement of an increase in the circulation of the deep vessels is not directly appraised by the methods in common use. The oscillometer measures pulsations in the large vessels. The plethysmograph cannot be easily adapted for routine clinical study. The muscle-temperature thermocouple is not useful for the measurement of the necessarily slow improvement that may occur. Skin-temperature measurements and immersion calorimetry deal essentially with changes in superficial vessels, and there is much evidence to indicate a dissociation in the response of deep and superficial vessels to drugs.²

The therapeutic agent tested in this study for its effect on circulatory function was testosterone propionate. The drug was first suggested by Arndt³ in 1939 for the relief of intermittent claudication. This author describes a favorable effect on this condition in 6 men, but the evaluation was based entirely on a general statement by the patient that he felt better. The duration of improvement was not given, and in 2 patients smoking was decreased or eliminated during the period of treatment.

Subsequently, Edwards et al.⁴ reported that testosterone produced "marked improvement in the walking ability of all the patients, with delay or abolition of the intermittent claudication." The patients were followed for several months, but no mention was made of other therapeutic procedures that may have been used simultaneously, nor was any objective measure of evaluation used.

In our study, the walking test was performed in a level, unobstructed hospital corridor, which was kept at a nearly constant temperature of 72°F during most of the year. An increase over this temperature in the summer did not seem to affect the performance of the patients.

They were paced at a constant rate of 88 yards a minute. In only 1 patient, who had definite peripheral arterial disease, was a faster pace necessary to bring on symptoms of claudication. They were asked to indicate, as they walked, the moment when tightness or cramps in the calf muscles appeared, but they continued to walk until the severity of the pain required them to stop. Those patients who at this moderate pace experienced angina pectoris or severe dyspnea before the onset of claudication were excluded from study.

Our series consisted of 6 men between the ages of forty-five and sixty-two years, all of whom had had intermittent claudication for from six months to seven years and were under observation in our clinic most of the time. One patient had thromboangitis obliterans, and the remainder had arterio-sclerosis; 1 of these also had diabetes mellitus. Each patient presented objective evidence of peripheral vascular disease: absent arterial pulsations, and color and temperature changes in the feet. Previous to observation, 2 had ceased smoking, and 2 had not, 5 had had Buerger's exercises, and 4 intravenous 5 per cent saline injections, with no defi-

*From the Departments of Medicine and Surgery, Beth Israel Hospital and Harvard Medical School.

†Assistant in Medicine, Harvard Medical School, junior visiting physician, Beth Israel Hospital.

‡Formerly assistant junior surgeon in the Out Patient Department, Beth Israel Hospital.

nite evidence of improvement subjectively or objectively.

In each case, a level walking test was performed weekly until three consecutive tests showed similar results. During the initial period of observation, all patients were given intramuscular injections of 1 cc. of physiologic saline solution. All other aspects of the care of these patients were unchanged, such as exercises and the use of tobacco and alcohol.

After a control period of four observations during at least one month, intramuscular injections of testosterone* were started. These were given three times a week—in 2 patients for six weeks, and in the remaining 4 patients for from three to six months. The total weekly dosage varied from 30 to 225 mg., averaging 100 to 125 mg. In addition to the intramuscular therapy, 3 patients were given the hormone by inunction daily for three weeks to a total dose of 50 mg.

In all the cases except one, the objective walking test showed no improvement in spite of occasional assertions of subjective improvement by the patient. This patient did not improve after doses of 15 to 150 mg. a week for ten weeks, but had a slightly increased walking tolerance after five additional weeks with doses of 225 mg. a week. The

The patients were not told the nature of the medication administered, but were questioned regarding possible effects of the treatment on sexual activity. One claimed an increased libido, but continued impotent.

DISCUSSION

Neither Arndt³ nor Edwards⁴ offered any explanation of the mechanism by which the improvement claimed from the use of testosterone was accomplished. Edwards et al.⁵ stated that there was an increase in oxygenation of hemoglobin in the cutaneous vessels of eunuchoids and castrates following the administration of androgenic substance. A possible explanation for the fact that some of their patients reported subjective improvement in walking ability is found in the recent reports that these preparations decrease muscular fatigability in eunuchoids.⁶ However, none of our patients with peripheral vascular disease and none of those of Arndt and Edwards exhibited any of the characteristics of testicular insufficiency. It is doubtful whether observations on eunuchoids or castrates can be applied to the normal elderly man.

SUMMARY

Measurement of a patient's ability to walk on a level surface at a given rate until the onset of claudication is a satisfactory method of evaluating peripheral circulatory function in ambulatory patients with peripheral vascular disease.

Using the above test, it was found that testosterone propionate, in dosages up to 150 mg. a week, did not prevent intermittent claudication in the lower limbs of 6 patients with occlusive vascular disease.

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TABLE 1. Influence of Testosterone Injections as Measured by the Walking Test.

SUBJECT	DURATION OF THERAPY wk.	ONSET OF PAIN trips	ENDURANCE OF PATIENT trips	DOSAGE OF TESTOSTERONE mg./wk.
CASE 1.	0	3	4	0
	8	2 1/2	3	0
	9	2 1/2	4	150
	11	2 1/2	4	50
	14	2 3/4	4	100
	27	3 1/2	3 3/4	100
CASE 2.	35	3	4	0
	0	1 1/3	2	0
	2	2	2 3/4	0
	4	1 3/4	2	0
	7	1 3/4	2	30
	26	1 3/4	2 1/2	75-100
	31	2	2 1/3	150

improvement was so slight that it was not deemed worth while to use such large and costly doses in the remaining patients. Table 1 shows the course of typical patients under this type of therapy.

*The preparation used, Oreton, contained 25 mg. of crystalline testosterone propionate to each cubic centimeter of sesame oil. This was generously supplied by the Schering Corporation, Bloomfield, New Jersey.

CLINICAL NOTES

HEMORRHAGE FROM A RUPTURED CORPUS LUTEUM*

REPORT OF A CASE IN A TWELVE-YEAR-OLD GIRL

PHILIP S FOISIE, MD†

BOSTON

INTRA-ABDOMINAL ovarian hemorrhage in nongravid patients has in recent years become recognized as a fairly common occurrence. Exclusive of cases due to a demonstrable lesion, there are a fairly large number in which hemorrhage of varying degrees occurs from apparently normal ovaries. These patients can be divided into two groups: those with a ruptured graafian follicle and those with a ruptured corpus luteum. The symptoms in these two groups differ chiefly in their relation to the menstrual cycle and in their severity. Rupture of the graafian follicle is a normal physiologic process that occurs in the mid-menstrual period and in which hemorrhage is rarely severe. Rupture of the corpus luteum is not physiologic, occurs in the premenstrual period and produces hemorrhage that may attain fatal proportions.

A review of the literature of the last fifteen years shows that there are now several hundred of such cases on record, with an age incidence anywhere during the childbearing period but rarely during the early years of that period. Hoyt and Meigs,¹ in 1936, reported a series of 58 cases, the youngest patient being fourteen years old. In the same year, King and Hawes² reported a case in a twelve year old girl in whom menstruation had begun one year earlier, at the age of eleven. The occurrence, therefore, of a case of hemorrhage of an exsanguinating degree in a girl of twelve whose catamenia began only a month before seems to be worth reporting to emphasize the necessity of considering this diagnosis at any time after puberty, even when the patient may be regarded as a child rather than a childbearing woman.

Before mentioning the details of this case, I shall review very briefly the normal physiology of ovulation. The ovaries are made up largely of a number of ova, and as any particular ovum matures, it approaches the periphery of the ovary, whose surface becomes prepared for its extrusion by a thinning-out process that reduces its vascularity. Physiologic rupture of the graafian follicle then occurs, with escape of the ovum, constituting ovulation and taking place at about the middle of the menstrual cycle. Usually, only a small amount

of serum escapes in this process, but sometimes a mild degree of bleeding also occurs that causes varying degrees of discomfort in the lower abdomen and not infrequently results in an erroneous diagnosis of acute appendicitis. Europeans seem to have more trouble with this condition than Americans; at least, it is talked of a good deal more in foreign literature and is what the Germans refer to as *Mittelschmerz*. Although varying degrees of hemorrhage may take place in this process, such bleeding rarely reaches alarming proportions, and conservative treatment is indicated.

Following ovulation, the ruptured graafian follicle seals up again and develops the yellow luteal cells that give it the name of corpus luteum. If impregnation does not occur, the corpus luteum rapidly degenerates, forming a white scar—the corpus albicans. Rupture of a corpus luteum causes hemorrhage that may reach fatal proportions. This occurs in the premenstrual period, a day or two before the onset of the next menses. Hemorrhage may be so extensive in these cases as to give signs of diffuse abdominal pain, nausea and vomiting, marked abdominal spasm and general evidence of severe blood loss. This picture is usually confused with that of a rupture in an ectopic pregnancy or in the less severe cases with acute appendicitis. The incidence seems to be definitely greater on the right side, and this, of course, adds to the confusion with appendicitis; moreover, symptoms are often referred to the right side even when the left ovary is involved.

The following case is interesting because the patient was a child whose catamenia had begun just one month before her illness. This patient had had only one previous corpus luteum that could have ruptured, and is therefore only one month removed from the earliest possible occurrence of the accident physiologically.

CASE REPORT

F O H (BCH 939366), a 12 year old girl was admitted to the hospital on May 7, 1939, with a complaint of abdominal pain. The first catamenia began 1 month before admission and lasted 5 days, with considerable cramps. The second period was due at the time of admission.

The patient had had measles, whooping cough and scarlet fever. The tonsils and adenoids had been removed 6 years previously.

The patient stated that the evening before admission she had a heavy supper consisting of baked beans, frankfurters, pickles, cake and milk, and that she awoke in the middle of the night with abdominal pain and nausea, she vomited about 4 a.m. and continued to be nauseated, and vomited during the rest of the night and the next morning. When she entered the hospital in the afternoon, it was stated that there were no abdominal signs. Examination of the urine showed 10 to 12 white blood corpuscles per high power field, and the patient was admitted on a medical service with a diagnosis of pyelitis. She continued to have abdominal distress and nausea, and gradually during the latter part of that day, abdominal

*From the Fourth Surgical Service, Boston City Hospital.
†Assistant in surgery, Tufts College Medical School; assistant to a consulting surgeon, Boston City Hospital.

signs became more apparent. Toward midnight, surgical consultation was requested, and I saw her about 1 a.m. The abdomen was distended throughout, with considerable spasm and marked tenderness in both upper quadrants, particularly the left. In addition, the patient presented the picture of acute blood loss. The blood pressure was 90/54. The red-cell count was 2,400,000 with a hemoglobin of 45 per cent, and the white-cell count was 17,000, with a shift to the left. The nonprotein nitrogen was 48 mg. per 100 cc. Examination of the urine showed an acid reaction, a specific gravity of 1.017, a + test for albumin and 10 white cells per high-power field. The vomitus showed a ++ test with benzidine.

Because of the unmistakable evidence of severe blood loss, the absence of any history of trauma and, most particularly, the onset in the premenstrual phase, a preoperative diagnosis of ovarian hemorrhage was made. The patient was given a 500-cc. transfusion, following which it was apparent that bleeding was continuing, and she was operated on about 3 a.m. under cyclopropane anesthesia. When exposed, the peritoneum was distended with dark blood, and the distention was so severe that this layer could not be picked up with an ordinary mouse-tooth forceps. When the abdomen was opened, large clots and free blood burst forth, thus giving evidence of old and fresh bleeding. The right tube and ovary were normal. The left ovary had been split wide open, so that only a shell remained. There was active bleeding from the inner surface of this shell. The ovary was clamped and removed, and the abdomen closed without drainage after all clots had been removed.

On the day following operation, the temperature rose to 104°F.; the pulse was 160, and the patient appeared to be moribund. She was put in an oxygen tent, two additional transfusions were given, and she promptly rallied. On the 3rd day after operation, she appeared to be definitely recovering. She made a normal convalescence and left the hospital in excellent condition on the 9th postoperative day.

This case could hardly have been distinguished preoperatively from a ruptured tubal pregnancy, except of course that the youth of the patient made this diagnosis improbable. It should be noted that Cullen's sign was not present, although the abdomen was extremely distended with dark clotted blood.

SUMMARY

The physiologically earliest case on record of intraperitoneal hemorrhage from ruptured corpus luteum is reported. It is emphasized that this condition must be considered in all females in the childbearing period who present acute abdominal signs.

Rupture of the graafian follicle, which is a normal physiologic process occurring in the midmenstrual period, may be accompanied by mild bleeding and may be confused with appendicitis.

Hemorrhage from a ruptured corpus luteum occurs in the premenstrual period and may be accompanied by severe hemorrhage, which may simulate almost any diagnosis connoting an acute

condition of the abdomen, most commonly acute appendicitis and rupture in an ectopic pregnancy.

520 Commonwealth Avenue

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THE USE OF SULFANILAMIDE FOR THE TREATMENT OF AN INFECTION DUE TO MICROAEROPHILIC STREPTOCOCCI

REPORT OF A CASE

ALFRED HURWITZ, M.D.*
AND EDWIN L. PRIEN, M.D.†

BOSTON

BURROWING subcutaneous infections caused by microaerophilic streptococci constitute a clinical entity characterized by extensive destruction and undermining of the skin and subcutaneous tissues. Topical antiseptics were found useless until Meleney¹ developed the zinc peroxide method of therapy.

The local use of chemotherapeutic agents has been described by Jensen, Johnsrud and Nelson² and Key and Frankel³ and has been employed with good results in the treatment of war wounds in England. Schneider⁴ successfully treated an undermining infection of the right thigh due to *Staphylococcus aureus* and microaerophilic streptococci with hydrogen peroxide and sulfanilamide locally. Meleney and Harvey⁵ reported favorable but not striking results with the use of zinc peroxide locally and sulfanilamide orally in the treatment of burrowing infections caused by *Streptococcus haemolyticus* of the microaerophilic type.

In the following case, the zinc peroxide method failed, but sulfanilamide powder rapidly effected a cure.

CASE REPORT

First admission. J. W., a 48-year-old man, was admitted on July 22, 1940, because of multiple draining sinuses in the left groin. The condition began as a small "pimple," which had been incised. A purulent discharge developed, and multiple sinuses soon formed. The condition became progressively worse. On admission, the patient presented an indurated area in the left groin, and the perineum contained multiple sinuses from which a profuse purulent discharge issued.

*Assistant in surgery, Harvard Medical School; assistant in surgery, Beth Israel Hospital.

†Associate neurologist, Newton Hospital; assistant neurologist, Boston Lying-in Hospital.

Cultures from the wound revealed diphtheroids, a non-hemolytic streptococcus, *Staphylococcus albus* and *Escherichia coli*. The Frei test for lymphogranuloma inguinale was questionably positive on one occasion, but negative when repeated. No tubercle bacilli or fungi were found. The blood Hinton and Kahn reactions were negative.

The clinical course was characterized by a low-grade fever not exceeding 100°F. The red-cell count was 3,500,000, and the white-cell count averaged 20,000. After 5 days of oral sulfanilamide therapy, extensive incision and drainage were performed. Boric acid dressings and irrigations were used postoperatively, and the wound gradually healed, so that after 55 days it was approximately half closed and covered by healthy granulation tissue.

The patient was discharged to his home under the care of a nurse, who continued the boric acid dressings. After 3 weeks, she noted that the wound failed to improve.

Second admission. When readmitted on October 31, the patient appeared chronically ill. The wound was covered with a dull-gray granulation, a purulent exudate escaping from beneath the skin margins. Undermining extended over a wide area from side to side, beginning at the left anterosuperior iliac spine and extending to the right beyond the right rectus abdominis muscle (Fig. 1) and from

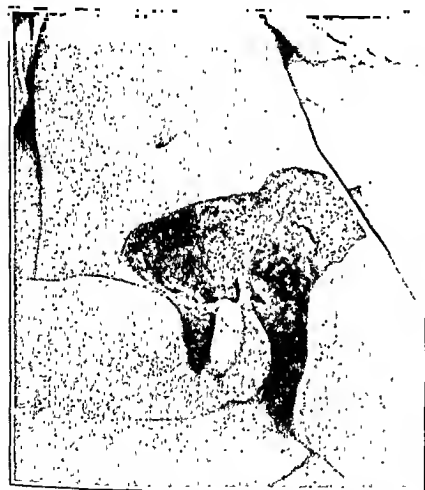


FIGURE 1. Wound after Radical Excision of Overlying Skin and before Sulfanilamide Therapy.

above downward beginning about 6 cm. below the umbilicus and extending over the medial aspect of the left thigh, including the area of the adductor canal and the tissue in the fold between the thigh and the scrotum as far back as the junction of the scrotum with the perineum. The process had also worked its way over the symphysis pubis in the midline and had invaded the areolar tissue between the symphysis and the dorsum of the penis so as to lay bare the sheath of the corpus spongiosum. A deep recess was formed in this way.

Laboratory data revealed a white-cell count of 18,300, a red-cell count of 3,470,000 and a hemoglobin of 58 per cent. Culture from the wound showed *Pseudomonas*

aeruginosa (*Bacillus pyocyaneus*) and, for the first time, a microaerophilic hemolytic streptococcus.

A radical excision was made with the electric cautery. The overhanging skin margins were excised back to healthy tissue except in the penile area, where little could be done except to widen the entrance to the recess. Both spermatic cords were uncovered. There was evidence of burrowing beneath the left cord, but no excision was made. In its widest extent, the wound measured about 28 cm. transversely. Most of the skin and subcutaneous tissue

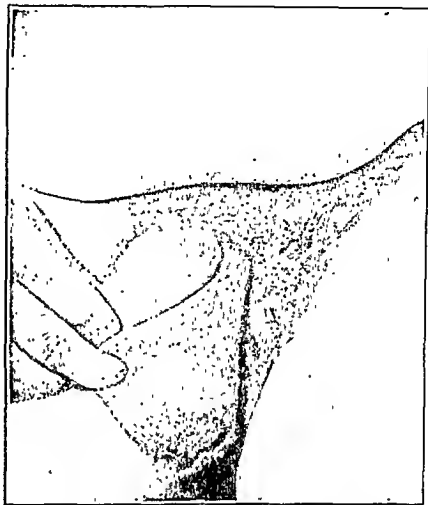


FIGURE 2. Wound about Six Weeks after Sulfanilamide Was Employed Locally and about Four Weeks after Grafting.

of the abdomen below the level of the umbilicus and of the medial aspect of the thigh over the adductor canal was removed. The pendulous portion of the penis sagged somewhat because its supporting tissues had been cut away, but the spermatic cords served to stabilize the penis and anterior scrotum.

Zinc peroxide dressings were applied daily, with considerable improvement at first. After several weeks of this treatment, it was found that the zinc peroxide was not being prepared according to the specific directions of Melency. This was remedied, but the lesion did not improve. The granulations became gray, and there was evidence of further burrowing of the process into the tissues about the left femoral artery in the groin. Anaerobic cultures were made through the courtesy of Dr. Champ Lyons, of the Massachusetts General Hospital, who reported that the hemolytic streptococcus did not belong to Group A, B or C of Lancefield and was therefore not likely to respond to sulfanilamide therapy.

On December 24, a spontaneous perforation of the left femoral artery occurred about 5 cm. below Poupart's ligament. Prompt action by an intern, who placed a clamp over the vessel just above the perforation, saved the patient's life. The artery was exposed with some difficulty because of the surrounding granulation tissue and was securely ligated. Transfusion of 1000 cc. of citrated blood from the hospital blood bank was given soon afterward.

The perforation had occurred above the junction of the profunda artery with the femoral, and the leg became cold rapidly. Paravertebral novocain block was not attempted because of the precarious condition of the patient. Fifteen hours after the accident, a line of demarcation appeared at the level of the mid-dorsum of the foot.

On the following day, the wound was sprayed with 2 gm. of sulfanilamide powder. This was repeated daily. Improvement was noted in the wound 24 hours after the first application of the powder. The granulations became red, and the wound closed in rapidly. After 2 weeks of sulfanilamide therapy, the wound was covered with pinch grafts, which were sprayed with sulfanilamide powder 48 hours afterward. Complete epithelialization was achieved after 6 weeks (Fig. 2).

On January 22, 1941, an open amputation of the toes and heads of the metatarsals of the left foot was performed because of gangrene and low-grade infection, and 2 gm. of sulfanilamide powder was sprayed into the stump tissues. A plaster-of-Paris shell was applied to immobilize the extremity. The foot dressing was left untouched for 9 days. Thereafter, the stump was sprayed with sulfanilamide powder about three times weekly. Sulfathiazole, 4 gm. daily, was started 2 days before the amputation was done and continued for 15 days. Thus, the patient

received sulfanilamide locally in the wound and sulfathiazole by mouth coincidentally. Convalescence was uneventful except for a pressure ulcer on the heel.

The patient was discharged improved on February 26. Since then, he has made steady progress.

SUMMARY

A case of infection due to a hemolytic streptococcus of the microaerophilic type and treated successfully with sulfanilamide locally after zinc peroxide therapy had failed is reported.

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MEDICAL PROGRESS

PHYSICAL THERAPY FOR DISEASES OF THE NERVOUS SYSTEM

ARTHUR L. WATKINS, M.D.*

BOSTON

THE treatment of patients with disorders of the neuromuscular apparatus constitutes a large proportion of the practice of physical medicine. The type of treatment used depends on the symptomatology present rather than the etiologic agent, since there are no specific curative physical measures. Consequently, diseases producing similar clinical symptoms and signs are grouped together, and the applicable physical-therapeutic measures outlined. The Kenny method of treatment of infantile paralysis has received so much publicity and interest that it is considered separately in more detail.

KENNY TREATMENT OF POLIOMYELITIS

The National Foundation for Infantile Paralysis has recently sponsored a course in physical therapy based on the Kenny method of treatment of infantile paralysis in the acute stage. This was given in Minneapolis by Drs. Cole, Knapp, Pohl and

others at the University of Minnesota. Sister Kenny and her associates demonstrated their method of treatment, and the original cases treated by her in this country were examined. This report is based on information obtained through this course and from the recent literature.¹⁻⁵

Before the results of the Kenny method are discussed, the traditional treatment of poliomyelitis, although not standardized, will be briefly outlined for the sake of comparison. The accepted opinion has been that, in poliomyelitis, flaccid paralysis of muscles occurs from destruction of the anterior-horn cells. In some cases, one group of muscles is thought to be more affected than its antagonist, so that the weaker muscles tend to be stretched by the pull of the stronger ones, with resulting deformities. The general principle of treatment is rest of the weak muscles by immobilization with splints designed to keep the stronger muscles stretched and to prevent tension on the weaker ones. Local applications of heat may be given one to three times a day in the acute stage to painful tender muscles. There is great variation in different institutions in the duration of the immobilization period. It may extend as long as eight weeks,

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. \$4.00).

*Assistant in medicine, Harvard Medical School; director of the Physical Therapy Department, Massachusetts General Hospital.

or in some cases, passive and active motion may be allowed from the beginning. When muscles are no longer tender, a detailed, functional muscle examination is done, and splints are adjusted to protect weaker muscles. Muscle re-education, which is then begun, consists of exercises designed to strengthen the weaker muscles with some active and passive painless stretching of the tight contracted muscles. This muscle training may be done on a table or under water, the splints being maintained between treatments.

The Kenny method of treatment is based on different concepts of the symptomatology and the factors that lead to the development of deformities. Sister Kenny admits that there will be a certain variable percentage of patients with a residual flaccid paralysis of one or more extremities. This is a result of complete anterior horn cell destruction, for which there is no known cure, and she does not claim cures. Her treatment is directed toward another condition, which she calls muscle 'spasm'. This symptom is thought to be of the utmost significance because, if it is not treated early, contracture, fibrosis, atrophy and loss of function result. This so-called "spasm" consists in pain, tenderness on pressure, constant hyperirritability particularly on stretching, and, in some cases, visible fasciculation. After several weeks, muscles that have been thus affected and not treated properly exhibit contracture, fibrosis and atrophy. Her term "spasm" refers in a general way to these conditions, and is misleading if interpreted according to accepted usage.

She has further observed that, in the majority of cases, the posterior muscles of the neck, trunk, and lower extremities are more affected by "spasm" than the anterior muscles with antagonistic action. She believes that the antagonists of the muscles with 'spasm', if treated in the traditional manner, become lengthened and atrophied from disuse, and finally, that power of voluntary contraction is lost. She designates such a functionally paralyzed muscle as 'alienated'. She also speaks of it as 'non-paralytic', meaning that if the "spasm" of its antagonist is released and it is allowed to regain its proper resting length it may be made to function by proper stimulation and re-education. She has learned to distinguish a truly paralyzed muscle from an "alienated" one by passively stretching the muscle repeatedly a few times within a small range of motion, then, by careful observation, a functionally paralyzed muscle will be seen to develop tension so that its tendon will stand out beneath the skin. One might explain this by the assumption that the myostatic stretch reflex had been thus elicited.

A third factor leading to muscular dysfunction has been described by Sister Kenny and called

inco-ordination. This consists in the substitution of accessory muscles or even antagonists for the proper prime movers of a joint. Individual muscles are also said to contract improperly in sections rather than through their full length, and again this is spoken of as "inco-ordination." This phenomenon, I believe, is at least in part generally recognized to occur whenever there is attempted motion of a joint by partially paralyzed muscles, particularly if such motion is painful, and also following immobilization.

The Kenny method of treatment aims to eliminate or correct these three factors leading to deformity and impaired movement. The muscle "spasm" must be treated as soon as the diagnosis is made. A delay of as little as three or four weeks may seriously compromise the results. Treatment consists in the application of hot packs of a measured size to fit muscles without immobilizing the joints. These woolen packs are immersed in boiling water, wrung out twice through a tight wringer at the bedside, and applied quickly to the involved part. The pack is then rapidly covered with oiled silk and a layer of dry flannel. The packs are changed every fifteen minutes if "spasm" is acute—otherwise, every two hours for a twelve hour period each day. Spasm is usually relieved within a week by such treatment, but packing is continued for weeks or months to any muscle exhibiting contracture or shortening. Although the original temperature is high, there is rather rapid cooling, and at the end of two hours there is probably a tendency for the body to heat the pack. This is in reality, then, a type of contrast therapy.

The patient is placed on a firm mattress with boards beneath and a piece at the foot of the bed so that the heels do not rest on the mattress. A footboard is provided, but the feet are not allowed to touch this so long as there is any 'spasm' of the gastrocnemius muscles. Later, the feet are placed firmly against the board, with pressure, to stimulate the standing reflexes.

No active or passive movements that cause any spasm or pain are allowed. When the "spasm" is relieved, only passive motions are started while the patient is still in the packs, and the muscles are said to be 'stimulated' by such motions. One might interpret this physiologically as setting up a barrage of proprioceptive impulses to facilitate the motor pathway and proper pattern of response. Active motion or muscle re-education begins only when 'spasm' has been relieved. This may be within a week in some cases, whereas in others, residual "spasm" in some muscles may require hot packs for months.

The Kenny system of muscle treatment sizes the isolated action of muscles for each joint.

exquisite control of agonists and antagonists so that smooth rhythmical motions are obtained. There is no effort to strengthen individual muscles by resistive exercises, but strength is increased by repeated co-ordinated movements. All the patients I saw in Minneapolis were beautifully trained in the performance of these motions and were flexible to a degree rarely seen in average normal persons.

The use of the respirator has been abandoned on the theory that the difficulty in breathing is due to the painful "spasm" of the pectoral and intercostal muscles, and with proper care of the airways and relief of the "spasm" by hot fomentations, spontaneous breathing is regained. Patients who do not respond to this and have complete paralysis or bulbar paralysis are not helped by the respirator in any event. The respirator precludes the use of hot packs and tends to increase the "spasm" by stretching the painful muscles. Careful nursing is particularly needed in these cases, and packs may be necessary during all waking hours. Moving pictures have demonstrated the effective relief of such "spasm" by packs and subsequent recovery. The contrast between patients treated by respirator and those treated by the Kenny method six months later is remarkable and the best argument for the latter treatment.

The most convincing evidence available at present in favor of the theory that untreated muscle "spasm" leads to contracture deformities is a comparison of the Kenny-treated patients with others in the same epidemic treated early by immobilization without packs. Whereas in the first group there was complete freedom of motion in all joints through a normal range, in the latter, a mild or marked degree of stiffness and contracture could be demonstrated, particularly of the posterior muscles of the back and lower extremities.

The nature of this muscle "spasm" or its mechanism of production is unknown, and at present no clinical or experimental studies have been completed. One may speculate on various possibilities. There may be a direct action of the virus or a toxin on the muscles, hyperirritability of affected anterior-horn cells, hypersensitivity to acetylcholine due to denervation, acetylcholine contracture, ischemic contracture or protective reflex spasm to avoid painful motion. The clinical impression that irreversible changes may occur if the patient is untreated for three weeks warrants investigation. One type of study that is easily carried out is electromyography. The most recent patient available in our clinic is being studied by this method. The onset of this patient's poliomyelitis was four months ago, and he now has partial paralysis of one shoulder girdle and upper arm. He was treated with an airplane splint and daily physical therapy in

the usual manner. The biceps, trapezius and pectoral muscles are now slightly shortened and tense, and occasionally show involuntary fasciculation. In maximum position of relaxation, the electromyographic tracings show marked electrical activity. This was lessened by thirty minutes of diathermy, according to a later observation. Some objective evidence that there is abnormal electrical activity in a muscle with "spasm" following poliomyelitis is thus demonstrated, although the mechanism is not explained.

The apparent paralysis or "alienation" of antagonistic muscles may be due to inhibitory pain reflexes, which are well recognized by physiologists. Immobilization is known to lead to atrophy and not infrequently to temporary loss of voluntary function. There may be, in addition, some actual weakness owing to partial anterior-horn-cell destruction. This should be ascertained in the future by study of electrical excitability and action potentials.

In one old case of infantile paralysis with a foot drop and an anterior tibial muscle rated as "zero," I stimulated this muscle with a faradic current, obtaining an excellent contraction. This tends to corroborate the Kenny theory that some of the paralysis observed is not due to anterior-horn-cell destruction.

Investigations are indicated to study the effect of hot packs and other forms of therapy on the nerves, muscles and circulation and to determine the most efficient method of treatment. The ritualistic tendencies of Sister Kenny are not conducive to this important research.

The Kenny method of muscle re-education seems an excellent one. The emphasis on stimulation of proprioceptive impulses as an aid to normal co-ordinated motion and control of relaxation and contraction of antagonists is probably on sound physiologic ground and much more so than immobilization with arrest of the flow of such impulses.⁶ Further study on this point may also evolve superior methods.

Results

It is extremely difficult to evaluate statistically the results of treatment in different groups of patients with poliomyelitis because of the variability in the extent of paralysis that is to be expected. Eighty-four patients in the early stage have been treated in Minneapolis by the Kenny method. Of these, there are residual paralyses in ten lower and two upper extremities. Although all patients showed involvement of the neck, back and hamstrings, in no case has there been residual trunk involvement. The most striking feature on observation of these patients is the *ease and co-ordination* of movement and the remarkable suppleness.

None of the familiar contracture deformities are seen, and the condition of the skin, subcutaneous tissues, muscles and joints in the extremities with paralysis is better than that in most cases, as judged by inspection and palpation. Although no splints or supports are used while "spasm" is present, they are not objected to after the period of convalescence. No deformities are observed because of this lack of immobilization. The comfort and morale of patients under treatment are impressive.

Conclusions

The Kenny treatment of poliomyelitis is not based on any new theory concerning the disease, but is essentially symptomatic treatment. Emphasis is placed on overcoming muscle pain, tenderness, hyperirritability and contracture. This is not done by immobilization, but by intensive early application of hot packs of a specified nature. As a result of this therapy, Sister Kenny has been able to start muscle re-education within a few days or weeks. Her system of re-education employs stimulation of proprioceptive impulses and training in co-ordination of individual muscle actions. Stiff joints, muscle contractures and disuse atrophy are largely eliminated when this treatment is started within the first two weeks or, preferably, as soon as diagnosis is made.

The functional results appear to be equal or superior to those by any known method of treatment. Although residual flaccid paralysis is not eliminated, a definite therapeutic contribution has been made.

Sister Kenny's attempted physiologic explanations in general have not been accepted. Clinicians and physiologists must further study neuromuscular mechanisms in this disease to place treatment on a rational basis and to determine the optimum methods.

PERIPHERAL NERVE INJURIES AND PERIPHERAL NEURITIS

Physical therapy physicians are frequently called on to aid in the diagnosis and prognosis of nerve injuries by special electrical examinations. The electrical excitability of muscles and nerves may be determined to give information concerning the degree of nerve injury to detect early signs of regeneration. The response to galvanic and faradic stimulation is the familiar test used, and the presence of a typical so-called "reaction of degeneration," as described by Erb, indicates a severe nerve injury. It is impossible, however, to predict that actual loss of continuity has occurred by a single examination of this type. One may have to wait for long periods to allow for possible spontaneous regeneration. Any test that will reveal regen-

eration at an early date is then of *clinical value*. The return of motor function is the most reliable sign of recovery.⁷ Although sensory changes may appear earlier, they are sometimes misleading because of overlap of sensory distribution from adjacent nerves. Tinel's sign may often be present in cases without regeneration. It has also been shown that the return of response to faradic stimulation may follow return of voluntary function.⁸ Recently, quantitative studies of electrical excitability by use of stimulating currents of measured strength and duration have been found to be of practical value.⁹ By repeated determination of strength-duration curves in affected muscles, the presence or absence of regeneration was detected before being noted by any other test.⁹

Proper splinting is essential in the care of peripheral nerve injuries. If the nerve has been sutured and contains motor fibers, the splint should prevent tension on the suture line. The muscles supplied by the injured nerve should be protected from the pull of their antagonists, and as much free active use as possible should be allowed. Harmer¹⁰ has described excellent splints for use in injuries of the wrist and hand. Heat and massage are indicated to improve circulation and thus lessen passive congestion and fibrosis. Great care must be taken in the application of heat to an area with impaired sensation. Diathermy is contraindicated because of the danger of burns. Immersion in warm water and application of radiant heat are simple, effective methods that have the added advantage of safe use in the home, with proper instructions. In massaging denervated muscles, one should employ only gentle stroking and kneading motions, with great care not to injure the delicate vessel walls and muscle fibers. Limited passive movements avoid undue stiffness of joints. Supervised graded active exercises are the most important aids in the recovery of muscle strength.

The value of electrical stimulation of denervated muscle to lessen atrophy and hasten regeneration has not been settled either clinically or experimentally. The studies of Chor et al.¹¹ on monkeys and Molander and Steinitz¹² on dogs indicate that electrotherapy adds little of practical value. Fischer,¹³ working with rats, used more intensive stimulation and did diminish the degree of atrophy. More recently, Gutmann and Gutmann¹⁴ repeated similar experiments on rabbits and continued their study to cover the period of regeneration. They found that daily stimulation with an interrupted galvanic current for fifteen to twenty minutes resulted in no difference in the degree of atrophy during the first two weeks. Subsequently, the treated muscles atrophied less and showed better excitability with stronger contractions. Al-

though the time of return of voluntary function was not affected, the strength and weight of muscles increased with greater rapidity, and this difference could be appreciated two months after the first return was noted. Biopsies showed larger muscle fibers and better striation. The clinical impression of many physicians has been that electrical stimulation is beneficial at least in maintaining the muscles in a receptive condition to the return of nerve fibers. A critical analysis of the clinical effects of electrical stimulation seems of definite value. The technic of stimulation commonly used may not be most advantageous. Some evidence has been presented by Liebesny¹⁵ that the progressive Leduc current is the most effective stimulus.

Electrical stimulation has been used more routinely in facial-nerve paralysis than in any other peripheral-nerve disorder. This may be because people are more concerned with appearance of the face than other portions of the body. The evidence for its value is largely that of clinical impression. Principles of treatment for any flaccid paralysis apply to facial muscles. Splinting, with either adhesive tape or insulated wire, extending from the corner of the mouth to the ear prevents overstretching from pull of the opposite side and of gravity. Local heat with an infrared lamp and gentle stroking improve nutrition and muscle tone. Electrical stimulation, if used, should be obtained with either an interrupted galvanic or an alternating current, such as a faradic or sinusoidal current. The latter is preferable if the excitability of the muscles is sufficient to allow contractions; if not, the galvanic current must be used. Repeated contractions are stimulated to the point of fatigue. In cases in which the facial nerve has been more severely affected, a period of approximately three months will elapse before the first signs of regeneration are noted. In these cases, it has been observed that recovery is never complete. The regenerating nerve fibers apparently divide in such fashion that, instead of allowing individual action of different groups of muscles, the entire facial musculature tends to contract as a whole. There is also spontaneous fasciculation, and a tendency to contracture. The treatment at this stage of recovery should be directed toward muscle re-education to acquire symmetric facial movements. Measures to ensure relaxation of muscles rather than stimulation are indicated. The simple application of local heat is beneficial, as is skillfully administered, sedative, stroking massage. Heavy massage and electrical stimulation should be avoided in the presence of spasm and abnormal associated movements.

In the physical therapy of peripheral neuritis, the same principles apply as in the treat-

ment of peripheral-nerve injuries. Usually, less rigid attention is paid to immobilization with splints and other appliances in view of the fairly good prognosis ordinarily given this disease. In some cases, pain is a distressing symptom and difficult to relieve. Infrared radiation frequently gives some temporary relief. Fever therapy has been used with apparent benefit in a few severe cases.¹⁶

SPASTIC PARALYSIS

A great variety of pathologic processes may result in spastic paralysis. Hemiplegia following a cerebrovascular accident or cerebral trauma is a familiar clinical syndrome, and definite improvement in function can be expected in most cases from proper physical measures.

Traumatic, neoplastic, degenerative and infectious spinal-cord lesions may produce spastic paralysis of one or more extremities. The treatment is essentially the same in these cases as in the cerebral ones. If there is marked sensory involvement as well, some alteration in treatment is necessary. When physical therapy is first started, there may be a complete flaccid paralysis, which gradually changes to a partial spastic paresis. During the flaccid period, stimulative massage and passive exercises may improve the condition of the extremities. With the appearance of spasticity, however, stimulative massage should be avoided and only mild stroking or very gentle kneading used, since the muscles are hyperirritable and spasticity may be increased and thus lessen function. Local heat either from a radiant source or from the use of hot baths, locally or generally, is of some value in reducing spasticity. Muscle re-education is the most vital procedure. Patients must be taught how to acquire maximum relaxation of the spastic muscles and to attain co-ordinated movement. Each case varies in the degree of involvement, and exercises must be adjusted accordingly. There is a tendency for flexion contractures to occur, and the use of night splints aids in their prevention. Mild passive stretching also helps to prevent joint stiffness. To obtain synchronous motions of several extremities and in acquiring skilled movements, occupational therapy is exceptionally valuable.

The treatment of infantile cerebral palsy has been elaborated in some detail by Phelps¹⁷ and others,^{18, 19} and is not discussed here. The general principles of treatment as outlined above are employed in these cases.

ATAXIA

Sensory loss from involvement of cerebral centers or spinal-cord tracts may be the most disabling feature in some cases of hemiplegia, posterolateral

sclerosis accompanying pernicious anemia, tabes dorsalis, multiple sclerosis and Friedreich's ataxia. In these cases, attempts are made to improve co-ordinated movement by special muscle re-education. Emphasis is placed on gaining control of position of the extremities through visual pathways, since the normal proprioceptive impulses are lacking. Such exercises have been outlined in some detail by Coulter.²⁰ When there is spasticity as well as diminished sensation, the measures described for its treatment may be combined. With proper instruction and supervised practice, the patient should learn to carry on a program of home therapy to obtain the best results. In diseases with a tendency to progressive loss of function, such as Friedreich's ataxia and multiple sclerosis, elaborate expensive programs should be avoided, for such treatment cannot affect the course of the disease.

MISCELLANEOUS CONDITIONS

Patients with muscular dystrophy, myasthenia gravis, myotonia, periodic paralysis and progressive muscular atrophy are sometimes subjected to physical therapy, including electrical stimulation and exercises. There seems to be no rational basis for such measures. The only physical agents of value are rest and instruction in good body mechanics. Mild massage is probably harmless, and in some cases of progressive muscular atrophy may be of definite psychotherapeutic value and tends to improve impaired muscle circulation. Conceivably, the extent of fibrillation might be reduced by local heat and sedative stroking, with a consequent delay in atrophy, but no effect on the neurologic lesion can be anticipated.

Backache and pains referable to other joints are frequent complaints of patients with paralysis agitans. The local use of heat is of value in the temporary relief of these symptoms. Such a simple remedy, which may be repeated frequently in the home, may be very comforting. Since these patients tend to remain immobile in a sitting position, they are greatly handicapped by their rigidity when they attempt to move. Supervised therapeutic exercises, including rhythmical motions or the use of music, may distinctly improve muscular performance.²¹

Hydrotherapy has a recognized place in the treatment of psychiatric conditions. A new edition of Wright's²² textbook on hydrotherapy covers the subject thoroughly.

Electric-shock treatment is the newest development in physical treatment of patients with manic depressive psychoses and dementia praecox. The latest reports²³⁻²⁵ agree largely with those previously reviewed²⁷ in that the best results are obtained in depressed patients. A report on a subconvulsive reaction to electric shock in a normal subject is of interest.²⁸ The extent of brain damage that may result from this treatment is still indeterminate because of lack of available material for study.

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND SIXTY-FIRST ANNIVERSARY

May 25, 26 and 27, 1942

THE one hundred and sixty-first anniversary of the Massachusetts Medical Society was observed in Boston on Monday, Tuesday and Wednesday, May 25, 26 and 27, 1942, at the Hotel Statler.

Fifteen hundred and fifty-six physicians and one hundred and twenty-three ladies were registered.

MONDAY, MAY 25

The annual golf tournament, under the chairmanship of Dr. Roy J. Heffernan, was held on Monday afternoon at the Commonwealth Country Club. There were twenty-four entries. The winners were as follows:

Low net (Burrage Bowl) — William R. Hill

Second low net — Hollis L. Albright

Third low net — Allen R. Barrow

Low gross — John J. Grinold

Second low gross — David P. Dutton

Third low gross — Roy J. Heffernan

The supervising censors met at 5:00 p.m. in the Hancock Room.

The Cotting Supper was served to 209 councilors in Parlors A, B and C at 6:00 p.m. The annual meeting of the Council was held in the Georgian Room at 7:00 p.m.

TUESDAY, MAY 26

A general clinical meeting was held in the Georgian Room in the forenoon under the co-chairmanship of Dr. Cadis Phipps and Dr. Edward J. O'Brien, Jr. The attendance varied from 250 to 600.

The one hundred and sixty-first annual meeting of the Society was held in the Georgian Room at 11:00 a.m. Dr. Ober, president of the Massachusetts Medical Society, presided. The attendance was about 650. The Annual Oration, "Some Remarks on Therapy for Anemia," was delivered at the close of the meeting by Dr. William B. Castle. During the course of the annual meeting, Dr. Ober introduced Dr. Forrest B. Ames, of Bangor, Maine, the only representative from other state societies present.

The annual luncheon was served in Parlors A, B and C to 190 fellows.

A clinical meeting was held in the Georgian Room from 2:00 to 5:00 p.m. under the co-chairmanship of Dr. George Leonard Schadt and

Dr. Ralph R. Stratton. The attendance was 600.

There was a reception and tea for the ladies in the Salle Moderne at 3:30 p.m. There were 62 ladies in attendance.

The annual dinner was held in the Georgian Room, at 7:00 p.m., with 506 in attendance. Dr. Frank R. Ober presided. Reverend Henry M. B. Ogilby pronounced the invocation. Dr. Frank H. Lahey, president of the American Medical Association, and Dr. Morris Fishbein, editor of the *Journal of the American Medical Association*, were the speakers. The Shattuck Lecture, "Medicine and Air Supremacy," was delivered immediately after the annual dinner by Dr. John F. Fulton, of New Haven, Connecticut.

The ladies' dinner was held at the Copley-Plaza at 7:30 p.m. There were 39 in attendance.

WEDNESDAY, MAY 27

There was a general clinical meeting in the Georgian Room from 9:00 a.m. to 12:00 noon under the co-chairmanship of Dr. Albert A. Horner and Dr. Edward P. Bagg.

Dr. Reginald Fitz and Dr. Frank H. Lahey discussed the Procurement and Assignment Service. Both answered many questions and emphasized the immediate need of the armed forces for doctors. They both agreed that this was not being met. They hoped that it would not be necessary to use other than voluntary means to supply this need.

The ladies held a luncheon at 1:00 p.m. at the Women's City Club of Boston. There were 49 present.

From 12:00 m. to 2:00 p.m. there was a series of section meetings and luncheons. The Section of Medicine and the Section of Surgery held a combined meeting in Parlors A, B and C under the co-chairmanship of Dr. Erwin C. Miller and Dr. Grantley W. Taylor. The attendance was 143. The Section of Pediatrics, Dr. Philip H. Sylvester, chairman, met at the Junior League, Zero Marlborough Street. The attendance was 42. The Section of Obstetrics and Gynecology met at the Women's Educational and Industrial Union, 264 Boylston Street, under the chairmanship of Dr. M. Fletcher Eades. The attendance was 70. The Section of Radiology and Physiotherapy met in Parlors D and E. Dr. Joseph H. Marks was the

chairman. The attendance was 44. The Section of Dermatology and Syphilology met in Parlor F and the Hancock Room. Dr. Arthur M. Greenwood served as chairman. The attendance was 36.

From 2:00 to 4:00 p.m. a general clinical meeting was held in the Georgian Room. Dr. Frederick J. Lynch presided. There was a symposium on minor psychiatric disturbances in war and civilian life from 4:00 to 5:00 p.m. This was the last exercise of the meeting. The attendance varied from 450 to 500.

There were 69 technical and 16 scientific exhibits. These exhibits were viewed by large numbers.

The motion pictures, as usual, attracted a large number of fellows.

The lists of admissions and deaths are appended, together with the official lists of officers, standing and special committees, councilors, censors and so forth.

MICHAEL A. TIGHE, *Secretary*

ANNUAL MEETING OF THE SOCIETY

The one hundred and sixty-first annual meeting of the Massachusetts Medical Society was called to order by the president, Dr. Frank R. Ober, in the Georgian Room, at 11:00 a.m. There were approximately 650 fellows present.

The Secretary offered the record of the last annual meeting as published in the *New England Journal of Medicine*, issue of July 3, 1941, and moved its acceptance. This motion was seconded by Dr. Arthur T. Ronan, and it was so ordered by vote of the Society.

The Secretary presented the changes in membership, as follows:

Membership of Massachusetts Medical Society, as of May 22, 1941 5652

Gains

New fellows	193
Restorations	17
	— 210

Losses

Deaths	109
Resignations	12
Deprivations	32
	— 153

Net gain 57

Membership, as of May 26, 1942 5709

The Secretary moved the acceptance of this report. This motion was seconded by Dr. William A. R. Chapin, and it was so ordered by vote of the Society.

Dr. Ober presented Dr. J. Harper Blaisdell, chairman of the Committee on By-Laws. Dr. Blaisdell moved the unanimous consent of the members present to make certain corrections in

the text as presented to each member. He explained that these corrections would in no wise affect the thought involved in the by-laws. They were offered for the purpose of improving the English and for the further purpose of making these by-laws consistent throughout. The corrections submitted by Dr. Blaisdell were as follows:

In Chapter III, Section 5, line 33, after the word "councilors" insert "elect," so as to conform with Section 6, line 13, of Chapter III.

Correct Chapter V, Section 3, beginning with line 9, to read "applicant subscribes to the by-laws of the Society and code of ethics of the Society and of the American Medical Association. . . ."

Correct Chapter V, Section 3, so that the paragraph beginning on line 13 shall read as follows: "He shall furnish each new fellow with a copy of the *Digest, By-Laws, Code of Ethics and Medical Defense Act* of the Society, and of the *Code of Ethics* of the American Medical Association."

In Chapter V, Section 3, the paragraph beginning on line 17 and ending with the word "examined," should be deleted to comply with the deletion of Section 4 in this same chapter as this section appeared in the original text.

Correct Chapter VI, Section 8, so as to read as follows: "The traveling and incidental expenses of the officers, of the committees of the Society elected by districts and of standing committees of the Society, on request, shall be paid by the Treasurer, on presentation of an itemized bill duly approved by the President."

Dr. Blaisdell's motion was seconded by Dr. George Leonard Schadt, and it was so ordered by the unanimous consent of the members.

The first four chapters of the text as submitted, with the corrections noted, were adopted by the members without dissent. The corresponding chapters of the by-laws as amended in 1941 were deleted by vote of the members without dissent.

Dr. Blaisdell moved the adoption of Chapter V of the text as submitted. This motion was seconded by Dr. William H. Allen.

Dr. Herrman L. Blumgart said he had serious misgivings in connection with Chapter V, Section 2(b). He added that the state government, through the Massachusetts Board of Registration in Medicine, decides on the professional competence of applicants, and to the Society is left the determination of the proper character of all such applicants. It seems clear, he continued, that this by-law provides for very careful supervision and screening of all applicants according to the judgment of the individual members of the committees, and by adding to all that, the requirement of practice in the United States for five years, a grave injustice will be done to certain applicants.

Dr. Joseph H. Pratt said that he was in agreement with Dr. Blumgart and that a great wrong will be done if properly qualified physicians are not permitted to join the Massachusetts Medical Society until five years have passed after they have

been accepted as qualified physicians by the Massachusetts Board of Registration in Medicine.

Dr. Oliver Cope said he thought that Section 2 (b) as it appears in the text was somewhat revolutionary in concept. He added that there were many objections to it. It indicated, he continued, that the membership committees of the district medical societies are incompetent to decide who should be taken into membership.

Dr. Robert B. Osgood expressed the thought that Section 2(b) as it appears in the text is un-American and that it is not appropriate coming at this time when we are trying to obtain unity.

Dr. Blaisdell said there was nothing revolutionary in Section 2(b) as it appears in the text. He quoted from the by-laws as amended in 1941 as follows:

An applicant for fellowship who is a graduate of a foreign medical school or college or a domestic medical school or college not on the list recognized by the Council or of a medical school no longer in existence, and who has practiced for a minimum of five years, shall apply for fellowship

He referred to Burrage's *History of the Massachusetts Medical Society* as explanatory of what was in the minds of the originators of the old by-law. He said that this history made it very clear that applicants for membership should have lived in a community sufficiently long to afford their conferees opportunity to pass on their standards of practice. He added that the supervising censors overwhelmingly supported a much more restrictive Section 2(b) than the one that appears in the text.

Dr. David L. Halbersleben wanted to know if it was possible for these men to become honorary members. He was answered in the affirmative.

Dr. George D. Henderson, a member of the Committee on Medical Education, spoke in agreement with Dr. Pratt and Dr. Blumgart.

Dr. John Fallon pointed out that if Section 2 (b) of the text was not accepted there would be a serious upset of other parts of the text as presented. He added that the Committee on By-Laws and the Council, in adopting Section 2 (b) of the text, felt it took about five years to really know what kind of medicine a fellow practiced.

Dr. Jacob Fine observed that since 1937 the Massachusetts Board of Registration in Medicine had licensed 250 graduates of foreign medical schools and of that number about 100 are now in practice in Massachusetts. He added that the number of these men who have not lived up to the professional and ethical qualifications of the Society is insignificant. He added further that these men would not be permitted to take their patients to hospitals unless they were members of the Massa-

chusetts Medical Society. The best opportunity in which to study such men would therefore be lost.

Dr. Blaisdell at this point, with the unanimous consent of the members, withdrew his motion to adopt Chapter V. He then moved to adopt Section 2 (b) of Chapter V of the text as presented. This motion was seconded by Dr. Albert A. Hornor.

At the request of Dr. Reginald Fitz, Dr. Blaisdell read Section 2 (b) of Chapter V of the text as presented. This section reads as follows:

(b) The secretary of a district society shall receive an application from a graduate of a discontinued medical school, a foreign medical school or any medical school not approved by the Council only when:

The applicant has possessed a license to practice medicine in the United States or its territories for at least five years. This license shall be verified by the district secretary and the data relating to it shall be recorded in the applicant's application blank;

The applicant has submitted with his application the name and address of a sponsor who is a fellow of the district society concerned; and

The sponsor has caused to be delivered by fellows of the Society to the secretary of the district society *confidential* written opinions on the qualifications of the applicant.

Dr. Ober, having appointed Dr. Fallon, Dr. Fitz, Dr. Allen G. Rice and Dr. Henry T. Hutchins tellers, called for a show of hands on the part of those who favored the adoption of Section 2 (b) of the text as presented. He then called for a show of hands on the part of those opposed.

He announced the vote as 198 for adoption and 147 against. He therefore declared Section 2 (b) of Chapter V as it appears in the text adopted.

Dr. Blaisdell moved the adoption of Chapter V of the text in its entirety. This motion was seconded by Dr. Charles D. McCann, and it was so ordered by vote of the members.

Dr. Blaisdell moved the deletion of Chapter V of the by-laws as amended in 1941. This motion was seconded by Dr. Peirce H. Leavitt, and it was so ordered by vote of the members.

Dr. Blaisdell moved the adoption of Chapter VI as presented in the text. This motion was seconded by Dr. Maurice Gerstein.

Dr. Chapin believed that the district treasurers should continue to collect the dues of the members of the Massachusetts Medical Society. He expressed his opposition to the chapter in the text that changed this arrangement.

Dr. Blaisdell asked for the unanimous consent of the members to withdraw his motion to adopt Chapter VI. This consent was granted.

Dr. Blaisdell moved that Section 5 of Chapter VI be adopted. This motion was seconded by a fellow. The vote which was taken by a show of hands was 191 for adoption and 40 against. Dr.

Ober announced that Section 5 of Chapter VI of the text was adopted.

Dr. Blaisdell moved the adoption of Sections 1, 2, 3, 4, 6, 7 and 8 of Chapter VI of the text. This motion was seconded by Dr. Horner, and it was so ordered by the vote of the Council.

Dr. Blaisdell moved the deletion of Chapter VI of the by-laws as amended in 1941. This motion was seconded by Dr. David D. Scannell, and it was so ordered by vote of the Council.

Dr. Blaisdell moved the adoption of Chapter VII of the text. This motion was seconded by Dr. Scannell.

Dr. Chapin expressed a wish to hear from Dr. Schadt on the last paragraph under Section 5. Dr. Ober invited Dr. Schadt to discuss this section.

Dr. Schadt directed the attention of the members to Section 5 of Chapter VII, which provides that the Committee on Nominations shall cause its report to be published in the notice of the annual meeting of the Council. He said that he was fearful that this departure from what had been the practice over the years would lead to a good deal of political campaigning. He expressed the hope that this section of the text would not be adopted.

Dr. Carl Bearse believed that Section 5 of Chapter VII of the text should be adopted. He pointed out that the election of the officers of the Massachusetts Medical Society was a most important matter and that the members of the Committee on Nominations should not be hurried, as they were then, in performing their most important duty. He added that the Committee on Nominations could meet more than once and this fact would be of great help to it in arriving at a proper choice.

Dr. Fallon agreed with Dr. Bearse. He added that the adoption of Section 5 of Chapter VII would bring these nominations out in the open.

Chapter VII was adopted by vote of the members.

Dr. Blaisdell moved the deletion of Chapter VII of the by-laws as amended in 1941. This motion was seconded by Dr. Leavitt, and it was so ordered by vote of the members.

Dr. Blaisdell moved the adoption of Chapter VIII of the text as presented. This motion was seconded by Dr. Leavitt, and it was so ordered by vote of the members.

Dr. Blaisdell moved that Chapter VIII of the by-laws as amended in 1941 be deleted. This motion was seconded by Dr. Chapin, and it was so ordered by vote of the members.

Dr. Blaisdell moved that Chapter IX of the text as presented be adopted. This motion was seconded by Dr. Bearse, and it was so ordered by vote of the members.

Dr. Blaisdell moved that Chapter IX of the by-laws as amended in 1941 be deleted. This motion was seconded by Dr. Leavitt, and it was so ordered by vote of the members.

Dr. Blaisdell moved that the by-laws as a whole, with the corrections noted, as they appear in the text before the body, be adopted. Dr. Leavitt seconded this motion, and it was so ordered by vote of the members.

Dr. James C. McCann moved that the President be instructed to express to the Commissioner of Insurance and his associates the appreciation of the Massachusetts Medical Society for their kind co-operation and help in establishing Massachusetts Medical Service. This motion was seconded by Dr. Blaisdell, and it was so ordered by vote of the members.

Dr. McCann offered the following resolution:

WHEREAS, The House of Delegates of the American Medical Association in special session in 1935 stated that it reaffirms, also, its encouragement to local medical organizations to establish plans for the provision of adequate medical services for all the people, adjusted to present economic conditions, by voluntary budgeting,

WHEREAS, The delegates amplified this statement in special session September 16 and 17, 1938, with the restrictive remark that "in addition to insurance for hospitalization your committee believes it is practicable to develop cash indemnity insurance plans to cover, in whole or in part, the costs of emergency or prolonged illnesses",

WHEREAS, Pursuant to this obligation thus imposed upon state and county medical societies they have so acted as to warrant the report that by the summer of 1941, there were twenty state medical societies that had taken some steps toward the introduction of a medical service plan to operate over the entire state" (1941 edition *Organized Payments for Medical Services*), and since nearly the entirety of effectively organized and planned service schemes have utilized the principle of medical service contracts (California, Michigan, Buffalo, Utica, North Carolina, Washington, Oregon, Pennsylvania, New Jersey, Massachusetts and others),

WHEREAS, These major experimenting groups have not found wholly valid or practical for effectively aiding the lower income groups, such restricting and restrictive statements relative to contracts coming from the House of Delegates (1938) as "your committee unanimously concurs in the suggestion and recommendation that the American Medical Association adopt the principle that in any plan or arrangement for the provision of medical services the benefit shall be paid in cash directly to the individual member," and such statements as that from the revised publication, 1941 *Organized Payments for Medical Services*, page 21, that "the attitude of the American Medical Association towards methods of payment of medical bills has been clearly defined. The position [is plainly stated] that benefits should be paid to the patients in cash in the same manner as premiums are collected from them",

WHEREAS, The empirical findings of the major experimenting groups that a medical service contract best serves the end of a more adequate distribution of needed medical care in a manner which effectually protects the

lower income groups against the mounting costs of medical care, and is directly in accord with the realistic attitude of the Massachusetts Commissioner of Insurance that the "capital" sustaining such plans with payments on the unit basis is not cash but the physician's service; and

WHEREAS, The statement of the House of Delegates September 16 and 17, 1938, that "your committee recognizes the soundness of the principles of the workmen's compensation laws" implies acceptance of the important compensation principle of arranging the delivery of complete service to the patient without additional charge by the doctor, and with payment of the physician from insurance funds, all of which is the essence of a medical-service contract; be it therefore

RESOLVED, That the state and county units of the American Medical Association in undertaking medical-service plans at the behest of the parent organization will have their hand supported if medical-service contracts, as well as cash-indemnity contracts, are given equally frank direct approval by the House of Delegates.

Dr. McCann moved that the delegates from the Massachusetts Medical Society be instructed to present this resolution to the House of Delegates of the American Medical Association at its meeting in June in Atlantic City. This motion was seconded by Dr. Schadt, and it was so ordered by vote of the members.

Dr. Fitz presented the following resolution:

WHEREAS, During the present national emergency there is urgent need for a large number of young medical officers to be enrolled from Massachusetts in the Medical Corps of the Army; be it therefore

RESOLVED, That the Massachusetts Medical Society in annual meeting assembled, respectfully requests that physicians residing in Massachusetts who wish to volunteer their services, who are American citizens, who have spent four academic years of thirty-two weeks each in a school legally chartered to teach the practice of medicine, who have received a diploma as a doctor of medicine from such a school, who have had at least a year's internship in a registered hospital and who are licensed to practice medicine in Massachusetts, be regarded as eligible for commission in the Medical Corps of the United States Army provided that they are declared available for this distinction by the local committees of the Procurement and Assignment Service for Physicians in the areas where they have legal residence, and by the Massachusetts State Committee of the Procurement and Assignment Service for Physicians; and be it further

RESOLVED, That copies of this resolution be sent to the Secretary of War, the Surgeon General of the United States Army, Mr. Paul V. McNutt, director, Office of Defense Health and Welfare Services, Dr. Frank H. Lahey, chairman, Directing Board, and Dr. Walter G. Phippen, chairman, First Corps Area Committee.

Dr. Fitz moved the adoption of the resolution. This motion was seconded by Dr. Charles E. Mongan, and it was so ordered by vote of the members.

The designated delegates from the other New England state medical societies were as follows:

MAINE: Dr. Forrest B. Ames, Bangor

NEW HAMPSHIRE: Dr. W. J. Paul Dye, Wolfeboro
Dr. Wallis D. Walker, Rye Beach

VERMONT: Dr. Clair D. Rublee, Newport

RHODE ISLAND: Dr. Charles A. McDonald, Providence
Dr. Joseph C. O'Connell, Providence

CONNECTICUT: Dr. Joseph A. LaPalme, Putnam
Dr. William J. German, New Haven

Dr. Ober sought to introduce each of these delegates. Dr. Forrest B. Ames, Bangor, was the only one to respond.

Dr. Ames said that, as a former member of the Massachusetts Medical Society, he was particularly pleased to have the privilege of bringing the greetings of the Maine Medical Association. He commented on the references which had been made earlier in the meeting to Massachusetts Medical Service and said that there was considerable interest in this subject in Maine. He invited the members of the Massachusetts Medical Society to the annual meeting of the Maine Medical Association to be held June 21, 22 and 23 at Poland Spring.

Dr. William H. Allen was recognized by the chair. He offered the following recommendation:

The supervising censors recommend that Chapter V, Section 2(a), as it relates to the timetable which governs graduates of approved schools in their applications for membership in the Massachusetts Medical Society, be waived in the interest of those who are either in or who have applied for commissions in the armed forces of our country. The Board of Supervising Censors further recommends that this regulation shall prevail only for the present emergency.

Dr. Allen moved the adoption of this recommendation. Dr. Mongan seconded the motion.

Dr. Ober told the members that a recommendation similar to this had been made to the Council at its meeting the night before, and the motion calling for its adoption had been ruled out of order. He added that the recommendation now before the meeting had been submitted to counsel and that the latter expressed it as his opinion that it was entirely proper for the members of the Society to adopt it.

The motion to adopt the recommendation was put and adopted without dissent.

The Secretary again appealed to the district secretaries to send in the names of their fellows who have entered the armed forces of the United States.

Dr. Frank R. Ober then reported on "The State of the Society" as follows:

It is the duty of the retiring president at the end of his term of office in report on the state of the Society.

The total membership is now 5709. The net gain in membership over last year is 57.

The Council has held four sessions, three regular and one special. The attendance of councilors at these meetings showed a slight falling off from the previous year. This is to be deplored. Members of the Council are elected to represent their districts, and it is therefore the duty of each councilor, as an officer, to attend the meetings of the Council and remain until adjournment takes place.

Ten district-society meetings were attended by the president. Since we now have a president-elect whose duty may be to assist the president, it seems desirable that the president-elect be invited to make at least half of these visitations, thus relieving a part of the president's burdens and giving the president-elect a better acquaintance with the members.

Last year three fundamental changes were made in the by-laws: the office of president-elect was created, the term of president was limited to one year, and provision was made for an executive committee of the Council.

The Executive Committee held its first meeting on June 23, 1941, and proceeded to organize. Dr. Walter G. Phippen, your last president, was invited to be present, since it was through his efforts that this committee was advocated. Dr. Phippen was asked to speak, and he outlined some of the possible functions and duties of this new committee. The new by-laws provided that an executive secretary might be elected by the Executive Committee. It was decided to elect the executive secretary at this meeting. In order that this committee might be kept active, it was voted that it could make decisions in emergencies, advise with the officers of the Society, discuss and approve *ad interim* appointments, and formulate matters of policy in the affairs of the Society before presentation to the Council. The Executive Committee also voted that all committees having important reports to make before the Council should first submit them to the Executive Committee for review and discussion. The discussion of the committee is then to be presented to the Council in a formal report, with the idea that its deliberations might be expedited.

The Executive Committee has held three regular meetings and five special meetings. The special meetings were called to consider matters of great importance to the Society as a whole. Two meetings were held for the purpose of discussing the proposed new by-laws; one for electing the board of directors of the Massachusetts Medical Service; and one to hear and discuss the report of the chairman of the Massachusetts Committee of the Procurement and Assignment Service.

The Society is particularly fortunate that the Council elected last year a secretary who is ideal for the job. Dr. Tighe has devoted a great deal of time to the performance of his duties. His records are kept as they should be; his counsel is wise; his devotion to the best interests of the Society cannot be surpassed; in fact, it would seem to me who has worked so closely with him that his main interest in life is what is best for the Society. We should congratulate ourselves that we have selected wisely and well in filling this important office. To him, I extend the heartfelt thanks of the Society.

Your able treasurer reports that the finances of the Society are in as excellent a condition as these precarious times will permit. The Society has received interest on all securities held (except as in 1940). There are difficulties in investing funds in safe securities except those of too long maturation and at too high prices. Short

first-class bonds are in demand at low returns but are safe. The collection of annual dues is not so well maintained as in 1940. There have been more requests for remission of dues than in the preceding year, in large part owing to the fact that an increasing number of our members are going into the armed services. The expenses of the Society from January 1 to May 1 have increased, owing in part to increased activities of the Society and in part to legal services. The Society is indeed fortunate that it has a treasurer who is so unselfishly devoted to our best interests. I thank him also for his support and wisdom in the able management of our financial affairs.

The standing committees have performed their duties efficiently and most satisfactorily.

The Committee on Ethics and Discipline is to be congratulated on its circumspect attitude and method of procedure dealing with those problems which came before it. Your president has attended nearly all the sessions and feels well repaid for the time spent and knowledge gained.

The Committee on State and National Legislation has not had much to do since the last annual meeting because the General Court did not meet this year. It is quite obvious that this committee has long been accustomed to limit a large part of its activities to the deliberations of the State Legislature. This should not be, because there are many problems that are being brought before Congress almost daily, a proper knowledge of which is often of the utmost concern to all of us.

The new by-laws provide for a new Committee on Legislation, whose duty should be to gather information about all matters of legislation, both state and national, in order that the Society may be apprised in due time, so that measures may be taken to support what seems to be good and to oppose when such matters do not seem best in the interest of the public welfare.

The Committee on Public Relations is one of the most important and most useful in the Society. It has been extremely useful in ironing out the plan for the Massachusetts Medical Service, before this plan was presented to the Council. Dr. Thomas H. Lanman resigned as chairman of the subcommittee that had charge of working out the details of the insurance corporation. Dr. James C. McCann was appointed to succeed him. This committee, under the able leadership of Dr. McCann, has done a superb piece of work in organizing the insurance plan for low-income groups. This plan was presented in full to the Executive Committee of the Council for consideration and review, and then was finally whipped into its present shape and accepted by the Council. The corporation, which consists of the members of the Executive Committee, elected the board of directors on May 6, and also the clerk, Mr. Edmund L. Twomey, who ably guided the subcommittee throughout the formative stages. I wish to express my deep appreciation in behalf of the Society to all those whose untiring efforts made the plan possible.

The Committee on Postgraduate Instruction conducted a very successful assembly in October, 1941. The attendance was much larger than in the two preceding years, and there was no financial loss. There was some curtailment of the extension courses, owing to the fact that there was no federal aid for the general courses.

The *New England Journal of Medicine* continues to maintain its high standards and growth. There has been an increase of 775 subscriptions to nonmembers of the Society. Sixty per cent of the papers presented to the

editorial board were accepted. The operating loss this year was \$16,513.78 (nearly \$4000 less than in the previous year), and is covered by your contribution to the *Journal* of \$17,400.

The Society is taking an active part in the war program. The Committee on Preparedness was set up, which has thoroughly studied, together with subcommittees in the district societies, the situation of the physicians in the Commonwealth with regard to civil and hospital needs and their availability for induction into the armed services of the country. The need for medical officers is very pressing owing to the rapid expansion of the Army and Navy. We all must be prepared to make great sacrifices if the United Nations are to win this most terrible war of all time.

A Committee on Rehabilitation was appointed. The object of this committee is to see that those draftees having remediable defects may be rehabilitated so that they will be fit for war service. The committee is functioning in conjunction with the selective-service authorities.

At the October meeting of the Council, it was voted that a committee be appointed to revise the by-laws of the Society. Such a committee was organized and began to function almost immediately. Frequent meetings were held by the committee. Your president and secretary attended practically all of these. Many hours were spent every week in the study and revision of the by-laws. The new by-laws were adopted at a special meeting of the Council held in April. The attendance at this meeting was 189. Every old by-law was considered thoroughly. The continuity was rearranged so that in the new by-laws there would be eliminated the necessity of searching through many pages for special by-laws, which obviously should be in one place. There was added a new standing committee, the Committee on Industrial Medicine. The Committee on Legislation was changed to an elected committee. All elected committees were grouped and put in a prominent place. Important changes in composition without changes in principle were also made. The set-up of the Committee on Membership was changed so that it would decide about membership in the Society. I wish to thank the Committee on By-Laws for its devotion to duty in producing your new by-laws.

Last year President Phippen suggested that it was time to think about changes in the headquarters of the Society. It is obvious that these quarters are inadequate for the conduct of the affairs of the Society. However, no move should be made by the Massachusetts Medical Society which would separate by any great distance the location of the Boston Medical Library from that of the headquarters, owing to the facts that the office of the *New England Journal of Medicine* is in the headquarters of the Society and that the facilities of the Boston Medical Library should be at the disposal of the *Journal*.

Dr. David Cheever, president of the Boston Medical Library, published a report in the April 30 number of the *Journal* showing the present condition of the library. The library had an investigation made by competent authorities on medical-library matters. This report shows that the library is now centrally located and has sufficient storage space for many years to come, but is understaffed because of lack of funds. It is my recommendation that some organized effort be made to help solve this situation.

The activities of the Massachusetts Medical Society are expanding more and more every year. It is necessary to support these activities by having committees chosen wisely. The officers of the Society are finding that more and more demands are being made on their time in order to manage its affairs properly.

I have endeavored at all times to work for the best interests of the Society as a whole to the end that every physician in the Commonwealth will realize more and more that he can depend on an organization which he can support and which will support him in his efforts to care for and guard the health of his patients.

May I now thank all those officers and committees who have performed their duties so faithfully and well. I also wish to express my heartfelt appreciation for the confidence that you, the members of the Massachusetts Medical Society, have placed in me during the past year.

Dr. Ober introduced Dr. William B. Castle, who delivered the Annual Oration, entitled, "Some Remarks on Therapy for Anemia" (published in the *New England Journal of Medicine*, issue of June 4, 1942).

Dr. Ober announced that the Council would reconvene at 2:45 p. m. in the Salle Moderne.

Dr. Mongan moved that a rising vote of thanks be extended to Dr. O'Halloran and his associates on the Committee of Arrangements for the fine program they had presented. This motion was seconded by Dr. Bearse and adopted unanimously in the midst of great applause.

Dr. Mongan moved a rising vote of thanks to Dr. Castle. This motion was seconded by Dr. Fallon and adopted with great applause.

Dr. Mongan commented on the importance of the work that had been accomplished in the year that had just come to a close. He called it a history-making year. He complimented the executive officers of the Society and moved that the members extend to them a rising vote of thanks. This motion was seconded and adopted with loud applause.

Dr. Ober called on Dr. Roger I. Lee, president-elect of the Society. Dr. Lee was not present.

Dr. Ober presented Dr. George Leonard Schadt, president of the Massachusetts Medical Society for the ensuing year. Dr. Schadt was greeted with great applause.

It was moved by Dr. Mongan and seconded by Dr. Fitz that the meeting be adjourned. The motion was adopted by vote of the members.

At 1:55 p. m. Dr. Ober declared the one hundred and sixty-first annual meeting of the Society adjourned.

MICHAEL A. TIGHE, *Secretary*

APPENDIX

ADMISSIONS RECORDED FROM MAY 22, 1941, TO MAY 26, 1942

YEAR OF ADMISSION	NAME AND RESIDENCE	MEDICAL SCHOOL
1942	Adams, Raymond Delney, Winchester	Duke
1941	*Adler, Eric David, Greenfield	University of Heidelberg
1941	Allen, Fred Harold, Jr., Boston	Harvard
1942	*Andosca, John Baptist, Mattapan	Royal College of Physicians and Surgeons London
1942	*Angyal, Andras, Worcester	University of Turin
1942	Ashley, Alva, Needham	Vanderbilt
1942	Bailey, Charles Cabell, Boston	University of Virginia
1942	*Barone, William Daniel, Winchester	Middlesex
1941	Barry, Thomas A., East Boston	Tufts
1941	Bedinger, Ada Doughty, Taunton	University of Pennsylvania
1941	*Bell, Solomon Z., Dorchester	Middlesex
1941	Belsky, John, Chelsea	Boston University
1942	Benedetti, Charles Carl, Hingham	Fahnestock
1941	*Bennett, Nathaniel Noah, Brookline	Middlesex
1942	Bergin, Joseph David, Worcester	Boston University
1941	*Bernstein, Siegmund, New Bedford	University of Vienna
1942	*Bialow, Solomon Philip, New ton Centre	Middlesex
1942	Blanchard, Stanley W., Boston	Tufts
1942	*Bloomenthal, Abraham Phillip, Waltham	Middlesex
1942	Bloomfield, Stanley T., Boston	Boston University
1941	*Blumenthal, Fred Ralph, Taunton	University of Berlin
1942	*Borenstein, Morris Victor, Springfield	University of Vienna
1941	*Boynton, George Hollis, Billerica	Middlesex
1942	*Branch, Dexter Roland, Lynn	New York University
1941	*Brick, Edward Jerome, Northampton	Middlesex
1942	Briere, Arnold Charles, Lynn	Tufts
1941	Broadhurst, Alice Mary, Watertown	Tufts
1942	Broady, Harold, Lowell	St. Louis University
1942	Brownlee, Robert Emery, Boston	Harvard
1942	*Buono, Charles Louis, Worcester	Middlesex
1942	Burke, Jacob B., Chelsea	Tufts
1942	Burke, John Edward, Cambridge	Tufts
1941	Carpenter, Frederick John, Pittsfield	McGill
1942	Cartier, Roland Rodolphe, Rutland	University of Montreal
1941	Casey, David Timothy, Cambridge	Tufts
1942	Chadwell, Virginia Towse, Swampscott	Boston University
1942	Chase, John Seaman, Brockton	Harvard
1942	*Chase, Louis Samuel, Cambridge	University of Berlin
1941	*Cohn, Ernst, Dorchester	University of Wurzburg
1941	Crosby, Walter Franklin, Sterling	Tufts
1941	Cutter, Edward Parker, Cambridge	Harvard
1942	*Denny Brown, Derek Ernest, Cambridge	Osaka University
1941	*Deutsch, Felix, Cambridge	University of Vienna
1942	Dexter, Lewis, Boston	Harvard
1942	*DiSalvo, Joseph John, Lawrence	Middlesex
1942	*Dobelle, Martin, Pittsfield	University of Chent
1942	*Douglass, Hector Bertram, Bridgewater	Middlesex
1942	Durfee, Marion Birch, Worcester	University of Colorado
1941	Eigner, Sidney, Lynn	Boston University
1942	Ernst, Robert Goodfellow, Springfield	Yale
1942	Evans, Frances Eugenia, Boston	Tulane University of Louisiana
1942	Fairbanks, Edward Joseph, Webster	Harvard
1942	*Felsen, Herman, Easthampton	Anderson College of Medicine, Glasgow
1942	Ferguson, Albert Barnett, Canton	Cornell
1942	*Finkelstein, Samuel Manuel, Dorchester	Middlesex
1941	Fiumara, Nicholas John, Boston	Boston University
1942	Flynn, Simon A., Boston	McGill
1941	Foot, Estelle, Waverley	University of Vermont
1942	Forster, Francis Michael, Wellesley	University of Cincinnati
1941	*Forti, Emilio, Chestnut Hill	University of Modena
1941	† Freund, Ernest, Boston	aguc
1942	Galuszka, Bronislav Andrew, Barre	Tufts

1941	*Gerbi, Claudio, Boston.....	Royal University of Milan, Italy
1942	Giddings, W. Philip, Boston.....	Harvard
1941	*Goldberg, Joseph, Malden.....	Middlesex
1942	*Goldfarb, Samuel, Onset.....	College of Physicians and Surgeons, Boston
1941	*Golickman, Louis, Whitinsville.....	Middlesex
1942	*Gould, Malvin, Jamaica Plain.....	Middlesex
1942	*Grandfield, Robert Francis, Sandwich.....	Middlesex
1941	Grover, Nathan Zachary, Springfield.....	Tufts
1941	Hagan, Cornelius E., Jr., Fall River.....	Medical College of Virginia
1941	*Haight, Meyer H., West Warren.....	Middlesex
1941	*Haines, George Arthur, Everett.....	Middlesex
1941	Hamel, Albert Gerard, Taunton.....	Georgetown University
1942	Hawes, Lloyd Elmer, West Somerville.....	Harvard
1941	Hight, Donald, Worcester.....	Harvard
1942	Hill, Edwin Valentine, Lexington.....	Tufts
1942	Hopkins, Elizabeth A., Boston.....	Tufts
1941	Hueber, John Wemyss, West Somerville.....	Tufts
1942	Hurlbut, Robert Satterlee, Cambridge.....	Harvard
1942	Hussey, Mae Grace Schissler, Quincy.....	University of Cincinnati
1942	Izenstein, Louis Arthur, Springfield.....	University of Cincinnati
1942	Jacob, Louise Hurst, Westboro.....	University of Colorado
1942	Jetter, Walter William, Hingham.....	University of Buffalo
1942	*Kaplan, Isadore, Chelsea.....	Middlesex
1942	*Karbowniczak, John Joseph, Jr., Lowell.....	Middlesex
1942	Katz, Kermit Harry, Dorchester.....	Boston University
1942	*Kelemen, George, Boston.....	University of Budapest
1942	Kelly, Francis James, Worcester.....	Hahnemann
1942	Kinney, Thomas D., Boston.....	Duke
1941	*Kleinhandler, Eugene, Pittsfield.....	University of Berlin
1941	Kopans, David Eli, Newton.....	Harvard
1941	Kowal, Anne Helene, Waverley.....	University of Michigan
1941	Lamisha-Smith, Vera, Swansea.....	College of Medical Evangelists
1941	*Landau, Irving Isaac, Billerica.....	University of Berlin
1941	*Landers, Thornton Ainsworth, Whitman.....	Middlesex
1942	*Lankenner, Peter Anthony, Worcester.....	Middlesex
1942	Leach, Harriet Peabody, Chelmsford.....	Yale
1941	Leary, Deborah Cushing, Jamaica Plain.....	Yale
1942	Leary, John Edward, Springfield.....	Tufts
1941	Leonard, Paul Charles, Dorchester.....	Tufts
1941	*Levi, Paolo, Watertown.....	University of Milan, Italy
1942	*Loker, William Wright, Framingham.....	Middlesex
1941	Lynch, John Bernard, Jr., Dorchester.....	Tufts
1941	Lyons, Arthur William, Brighton.....	Tufts
1942	*Macdonald, Martin Luther, Waltham.....	College of Physicians and Surgeons, Boston
1941	Macklin, James Joseph, Jr., Cambridge.....	Tufts
1941	Magnet, Isaac Harry, Lee.....	Tufts
1941	Magnuson, Paul Lassonde, New Bedford.....	New York University
1941	Marcoux, William George, Melrose.....	Tufts
1942	Marnane, Joseph Patrick, Gardner.....	Tufts
1941	*Mazzolini, Andrew, Holyoke.....	Middlesex
1941	McAlpin, Kenneth Rose, Williamstown.....	Columbia University
1941	McCollum, Donald C., Brookline.....	George Washington University
1942	*Meinhardt, Charles, Malden.....	College of Physicians and Surgeons, Boston
1941	*Merzbach, Peter Francis, Cambridge.....	University of Frankfurt, Germany
1942	Messina, Salvatore Joseph, Somerville.....	Boston University
1941	Mezer, Jacob, Brookline.....	Tufts
1942	Mikalonis, Joseph Paul, Dorchester.....	Tufts
1942	Miller, Lois Cowan, Roxbury.....	University of Pittsburgh
1942	*Milone, Antonio Peter, Roslindale.....	Middlesex
1942	Moher, James Joseph, Lynn.....	Yale
1941	Mooney, Daniel Leo, Fall River.....	Harvard
1942	Mulligan, Francis Joseph, Newton.....	Boston University
1942	Mullowney, James Philip, Worcester.....	Loyola University
1942	*Nelson, Charles Edward, Lawrence.....	Middlesex
1941	Neuhauser, Edward B. D., Cambridge.....	University of Pennsylvania
1942	*Newlander, Harold, Malden.....	Middlesex
1941	*Nobili, Conrad, Quincy.....	Royal University of Rome
1941	*Nossiff, George Seavey, Milford.....	Middlesex
1942	O'Brien, David Francis, Somerville.....	Harvard

1942	Ohrenberger, Henry Wendell, Dorchester	Tufts
1941	*Ornstein, Frank Edward, Arlington	University of Vienna
1942	*Pallotte, John James, Essex	Kansas City University of Physicians and Surgeons
1942	Palmieri, Salvatore, Boston	Tufts
1941	*Picard, Julius, Fall River	University of Heidelberg
1941	*Portman, Abraham, Islington	Middlesex
1942	Rattigan, John Patrick, Hyde Park	Boston University
1941	*Redlich, Frederick Carl, Boston	University of Vienna
1941	Rhineclander, Frederic William, 2nd, Jamaica Plain	Harvard
1941	*Richards, Hazel Hortop, Malden	Middlesex
1942	Rissler, Ross William, Brighton	Indiana University
1941	*Rinkel, Max, Brookline	Christian Albrecht University
1942	Rnbbins, Laurence Lamsnn, Cambridge	University of Vermont
1941	*Robinson, Joseph, Hyannis	Middlesex
1941	Ross, Joseph Foster, Brookline	Harvard
1941	*Rothschild, Karl, Malden	University of Munich
1942	Rowe, Winston Judd, Natick	Tufts
1942	Runci, Dominic, Winchester	Middlesex
1942	Runge, Paul Martin, Brockton	Boston University
1942	Sabbagh, Joseph Najeab, Lawrence	Boston University
1941	*Salomon, Adolph, Williamstown	University of Frankfurt
1942	Saltzman, Charles, Harding	Boston University
1941	Sanborn, Frederick, Pocasset	Harvard
1942	Santacross, Nicholas Lewis, Jr., Milton	Harvard
1941	Sarris, Spiros Peter, Lynn	Harvard
1941	*Savignac, Raymond Joseph, Worcester	Strasbourg University
1941	*Schlomer, George Max, Georgetown	University of Munich
1941	Schoenbaeh, Emanuel Barnett, Boston	Harvard
1942	Scuto, Joseph Alfred, New Bedford	Hahnemann
1941	Settlage, Arnold Frederick Ernest, Newburyport	Harvard
1942	Shapiro, Morris William, East Gardner	Tufts
1942	Sherman, David S., Brookline	Boston University
1941	Sicard, Louis Adnen, Lowell	Tufts
1942	Silverman, Samuel, Dorchester	Harvard
1942	Silverstein, Louis Basil, Waltham	Boston University
1941	Simeone, Fiorindo Anthony, Brookline	Harvard
1941	*Slate, Benjamin, Cambridge	Middlesex
1942	Smith, Helen Olivia Price, Waltham	Boston University
1941	Smith, Robert Moors, Cohasset	Harvard
1941	*Sobel, Harry, Hyannis	Middlesex
1942	Soutter, Lamar, Boston	Harvard
1942	Stellar, Lawrence Irving, Newton Highlands	Tufts
1942	Stewart, Charlotte A., Harding	Yale
1942	Stone, Nathaniel Maurice, Brookline	Tufts
1942	*Sulzbach, Wolfgang Max Ferdinand, Waverley	University of Bonn, Germany
1941	Swan, Daniel Mason, Quincy	University of Rochester
1942	*Teed, Roy Wilham, Milford	Middlesex
1941	*Tell, Abram Batt, Worcester	Kansas City University of Physicians and Surgeons
1942	Tighe, Thomas James Gasson, Lowell	Harvard
1942	Tracey, Martin L., Brookline	Jefferson Medical College of Philadelphia
1941	Tripp, Edwin Prescott, Jr., Falmouth	Jefferson Medical College of Philadelphia
1942	*Tulloch, Prescott Ellis, Somerville	Middlesex
1942	Van Huysen, William Theodore, Weston	Tufts
1942	*Warburton, Norman Wilson, New Bedford	Middlesex
1941	Ward, Arthur Downing, Worcester	Tufts
1942	Weiner, Abraham Alfred, Saugus	Middlesex
1941	Whitcomb, Austin Elwood, South Hadley Falls	Columbia University
1942	*White, Seymour James, Lawrence	University of Paris
1941	White, Thomas Paul, West Newton	Tufts
1942	Wies, David, Waverley	Tufts
1942	Yovino, Emanuel M., South Boston	Tufts
1941	Zeller, John Wallace, Boston	Harvard

Total number of new fellows admitted	December, 1941	86
Total number of new fellows admitted	May, 1942	107

Grand total

193

*The cand date after a personal interview was approved by the Committee on Medical Education and permitted to take an examination before a board of censors

†Deceased

76

DEATHS REPORTED FROM MAY 22, 1941, TO MAY 26, 1942

ADMITTED	NAME	PLACE OF DEATH	DATE OF DEATH	AGE
1894	Albee, George MacDonald.....	Worcester	August 10, 1941.....	70
1903	Alexander, Thomas Branch.....	Scituate	August 28, 1941.....	65
1940	Anderson, Bertha Olive.....	Pittsfield	June 25, 1941.....	58
1899	Andrews, Harold Virgil.....	Boston	June 9, 1941.....	68
1927	Baker, Norman Clyde.....	Lexington	July 31, 1941.....	58
1938	Baldauf, Leon Kahn.....	Waltham	April 30, 1942.....	64
1892	Barnes, Francis John.....	Cambridge	April 28, 1942.....	79
1900	Barnes, James Arthur.....	Worcester	September 6, 1941.....	69
1905	Bartlett, Walter Oscar.....	Boston	November 5, 1941.....	62
1898	Benson, Charles Sweetser.....	Haverhill	April 30, 1942.....	69
1933	Bianco, Joseph Anthony.....	Boston	May 23, 1941.....	59
1924	Blackfan, Kenneth David.....	Louisville, Kentucky	November 29, 1941.....	58
1904	Blake, Allen Hanson.....	Somerville	December 9, 1941.....	60
1906	Blake, Gerald.....	Brookline	July 28, 1941.....	61
1903	Bonney, Robert.....	East Boston	March 22, 1942.....	83
1894	†Bragg, Francis Adelbert.....	Foxboro	February 6, 1942.....	77
1928	Breen, John Joseph.....	Lowell	February 3, 1942.....	39
1917	†Briggs, Joseph Emmons.....	St. Petersburg, Florida	January 3, 1942.....	72
1884	Brown, George Artemas.....	Barre	March 15, 1942.....	84
1897	†Burnett, Frank Hollis.....	Brockton	June 21, 1941.....	75
1892	†Burns, Hiram Hutchins.....	Plymouth	May 10, 1941.....	85
1905	Celce, Frank Frederick.....	Holyoke	April 28, 1942.....	74
1903	Cholerton, Herbert.....	West Somerville	September 25, 1941.....	68
1902 } 1924 }	Chrystal, Michael Henry.....	Leominster	July 13, 1941.....	73
1904	Clarke, Inez Louise.....	Cambridge	March 7, 1942.....	Unknown
1914	Cook, James Henry.....	East Hampstead, New Hampshire	March 28, 1942.....	58
1898 } 1903 }	Coon, George Bailey.....	Greystone Park, New Jersey	January 18, 1941.....	72
1889	†Craig, George Arthur.....	Swampscott	October 24, 1941.....	78
1913	Dalton, Charles Howard.....	Somerville	February 12, 1942.....	65
1895	Damon, Arthur Llewellyn.....	North Wilbraham	April 30, 1942.....	74
1906	†Davis, Minot Flaggs.....	Cambridge	July 26, 1941.....	79
1884	Delahanty, William Joseph.....	Worcester	May 10, 1942.....	84
1893	DeLue, Frederick Spaulding.....	Boston	March 17, 1941.....	72
1936	Diez, Mary Luise.....	Boston	April 12, 1942.....	63
1931	Dougherty, Harry Lawton.....	Boston	June 1, 1941.....	42
1922	Downey, Hugh James.....	Pittsfield	January 31, 1942.....	59
1935	Edgar, William Ladell.....	Athol	October 11, 1941.....	69
1899	Fair, John Francis.....	Cambridge	May 20, 1941.....	72
1906	Field, Henry Martyn.....	Norwood	May 20, 1942.....	67
1928	Flagg, Franklin Ivan.....	Boston	October 10, 1941.....	54
1903	Fleming, Peter Joseph.....	Jamaica Plain	December 15, 1941.....	66
1894	†Frame, Joseph.....	Rockland	May 24, 1941.....	75
1941	Freund, Ernest.....	Boston	February 19, 1942.....	64
1907	Fuller, Ernest.....	Lawrence	September 14, 1941.....	68
1901	†Galvin, William.....	North Adams	April 8, 1942.....	83
1933	Gilman, Bernard Barrett.....	Boston	May 31, 1941.....	37
1900 } 1926 }	Goodwin, Harold Carl.....	Springfield	March 1, 1942.....	63
1935	Haigis, Peter J.....	Foxboro	June 2, 1941.....	68
1901	Hartwell, William Winn.....	Malden	March 1, 1942.....	68
1915	Hersam, Norman Paul.....	Stoneham	January 15, 1942.....	57
1894	Higgins, James Haydn.....	Marston's Mills	April 7, 1942.....	71
1895	†Hopkins, Frederick Eugene.....	Springfield	July 1, 1941.....	83
1903	†Hurwitz, Abraham Joseph.....	Brookline	July 30, 1941.....	66
1920	Johnson, Elmon Reuben.....	Wollaston	October 30, 1941.....	70
1896	Kelleher, Patrick Francis.....	Cambridge	September 25, 1941.....	73
1927	Krantz, Michael.....	Forest Hills	September 4, 1941.....	54
1900	†Ladd, Maynard.....	Media, Pennsylvania	March 9, 1942.....	69
1884	†Lane, Edward Binney.....	Milton	September 17, 1941.....	81
1895 } 1917 }	†Leach, Albert Clinton.....	Orange	November 9, 1941.....	70
1927	Leonard, John Michael.....	Fall River	October 26, 1941.....	65
1902	Lord, Frederick Taylor.....	Boston	November 4, 1941.....	66
1933	Lord, William Ogden.....	New Bedford	August 8, 1941.....	60
1924	Lourie, Osip Raphael.....	Boston	October 27, 1941.....	68

1906	Macdonald, Frederick Cornelius	Boston	October 27, 1941	65
1891	Mallory, Frank Burr	Brookline	September 27, 1941	78
1933	Manning, Arthur Francis	Waltham	December 12, 1941	39
1897	Martin, Archibald Herbert	Boston	December 13, 1941	69
1884	†Mason, Atherton Perry	Fitchburg	October 20, 1941	85
1930	McCrossan, Charles Leo	Somerville	June 26, 1941	55
1927	Meledy, Joseph Aloysius	Washington, D C	April 1, 1942	50
1932	Mulholland, Bernard Joseph	Lawrence	April 16, 1941	57
1903	Murphy, Daniel David	Boston	August 8, 1941	75
1936	Mutty, Lawrence Theodore	Boston	February 25, 1942	36
1929	Niwarro, Vicente Aguirre	Medfield	May 15, 1941	45
1900	Norton, George Paul	Fitchburg	June 12, 1941	67
1935	O'Leary, Cornelius Joseph	Brighton	May 20, 1942	39
1937	Osborne, Edward Daniel	New Bedford	May 18, 1941	64
1908	Perry, Sherman	Winchendon	April 20, 1942	63
1928	Peters, Andrew	Springfield	January 8, 1942	51
1887	†Pope, Frank Fletcher	Ashby	August 27, 1941	82
1901	Potter, Alexander Carleton	Cambridge	January 28, 1942	68
1905	Powers, George Herman	Boston	October 4, 1941	64
1898	Reed, Victor Augustus	Methuen	February 24, 1942	73
1941	Rhees, Morgan John	Wabun	August 25, 1941	41
1935	Ring, Barbara Taylor	Arlington	August 31, 1941	61
1906	Rogers, Mark Homer	Boston	October 5, 1941	64
1896	†Ryan Dennis Matthew	Ware	June 14, 1941	81
1891	†Sawyer, Walter Fairbanks	Fitchburg	December 9, 1941	73
1887	Sears, Henry Francis	Boston	January 1, 1942	80
1903	Sise, Lincoln Fleetford	Brookline	April 28, 1942	67
1898	†Smith, Alfred Charles	Brockton	July 15, 1941	72
1886	†Stone, Frank Ellsworth	Lynn	September 3, 1941	79
1891	Stowell, Edmund Channing	Merrillboro New Hampshire	December 20 1941	65
1907	Swift, Walter Babcock	Boston	May 2, 1942	74
1902 } 1915 }	Tabor, Edward Orlando	Lowell	August 25, 1941	65
1893	Ten Broeck, Stanton Jacob	Orange	January 14, 1942	70
1880	†Tobey, George Loring Sr	Medonak, Maine	September 18 1941	88
1905	Tracy, John Mathew	Springfield	July 9 1941	72
1910	Tracy, William Leighton	Pittsfield	August 2, 1941	66
1930	Tully, George William	Southbridge	July 21, 1941	53
1928	Tuttle, George Herman	South Acton	April 2, 1942	76
1919 } 1939 }	Vickery, Eugene Augustus	Wellesley	June 22, 1941	62
1892	†Vickery, Lucia Florence	Jamaica Plain	October 23 1941	81
1930	Wakefield, Arthur Paul	Belmont	February 6 1942	63
1920	Walsh, James Henry	Fall River	May 14, 1941	57
1878	Watson Francis Sedgwick	South Dartmouth	May 5, 1942	88
1927	Weiss, Soma	Boston	January 31, 1942	43
1882 } 1888 }	†Wood, Henry Austin	Waltham	February 22 1942	86
1905	†Young, Roy Demas	Arlington	July 25, 1941	70

†Retired fellow

Total number of deaths of active fellows	85
Total number of deaths of retired fellows	24
Grand total	109

OFFICERS FOR 1942-1943

PRESIDENT George Leonard Schadt, Springfield 44 Chestnut Street.
 PRESIDENT ELECT Roger I Lee, Boston, 264 Beacon Street
 VICE PRESIDENT Peirce H Leavitt, Brockton 129 West Elm Street.

SECRETARY Michael A Tighe, Lowell Office, Boston 8 Fenway
 TREASURER Charles S Butler, Boston, 257 Newbury Street
 ASSISTANT TREASURER Eliot Hubbard, Jr., Cambridge 29 Highland Street.
 ORATOR Edward P Bagg, Holyoke 207 Elm Street

EXECUTIVE COMMITTEE OF THE COUNCIL

Members Ex-Officiis

PRESIDENT: George Leonard Schadt, Springfield, 44 Chestnut Street.
 PRESIDENT-ELECT: Roger I. Lee, Boston, 264 Beacon Street.
 VICE-PRESIDENT: Peirce H. Leavitt, Brockton, 129 West Elm Street.
 SECRETARY: Michael A. Tighe, Lowell. Office, Boston, 8 Fenway.
 TREASURER: Charles S. Butler, Boston, 257 Newbury Street.

Term Expires 1943

BARNSTABLE: William D. Kinney, Osterville*
 BRISTOL NORTH: William H. Allen, Mansfield, 70 North Main Street. (Alternate: Ralph M. Chambers, Taunton, Taunton State Hospital.)
 BRISTOL SOUTH: Edwin D. Gardner, New Bedford, 150 Cottage Street.
 ESSEX NORTH: Frank W. Snow, Newburyport, 24 Essex Street. (Alternate: Rolf C. Norris, Methuen, 247 Broadway.)
 MIDDLESEX EAST: Kenneth L. MacLachlan, Melrose, 1 Bellevue Avenue. (Alternate: Richard Dutton, Wakefield, 33 Avon Street.)
 PLYMOUTH: Peirce H. Leavitt, Brockton, 129 West Elm Street. (Alternate: George A. Moore, Brockton, 167 Newbury Street.)

Term Expires 1944

BERKSHIRE: John J. Boland, Pittsfield, 334 North Street.
 FRANKLIN: Frederick J. Barnard, Greenfield, 479 Main Street.
 HAMPSHIRE: George L. Steele, Springfield, 20 Maple Street.
 MIDDLESEX NORTH: William M. Collins, Lowell, 174 Central Street.
 NORFOLK: Carl Bearse, Boston, 483 Beacon Street.
 WORCESTER NORTH: John J. Curley, Leominster, 82 Main Street.

Term Expires 1945

ESSEX SOUTH: Loring Grimes, Swampscott, 84 Humphrey Street. (Alternate: Charles L. Curtis, Salem, 10 Federal Street.)
 HAMPSHIRE: L. Beverly Pond, Easthampton, 115 Main Street.
 MIDDLESEX SOUTH: Not yet elected.
 NORFOLK SOUTH: Daniel B. Reardon, Quincy, 1186 Hancock Street.
 SUFFOLK: Donald Munro, Boston, 818 Harrison Avenue. (Alternate: Charles C. Lund, Boston, 319 Longwood Avenue.)
 WORCESTER: Ralph S. Perkins, Worcester, 10 Hackfeld Road.

STANDING COMMITTEES FOR 1942-1943

ELECTED BY THE COUNCIL, MAY 25, 1942

Date of Appointment

COMMITTEE ON PUBLICATIONS — Established 1825.

R. M. Smith	June 6, 1933 (appointed chairman May 21, 1941)
J. P. O'Hare	June 9, 1936
Conrad Wesselhoef	June 2, 1937
W. B. Breed	February 7, 1940
Oliver Cope	May 21, 1941

COMMITTEE ON ARRANGEMENTS — Established 1849.

G. M. Morrison	May 21, 1941 (appointed chairman June 24, 1942)
R. J. Heffernan	May 25, 1942
S. C. Wiggin†	June 24, 1942
R. H. Barker†	June 24, 1942
R. I. Smith†	June 24, 1942

COMMITTEE ON ETHICS AND DISCIPLINE — Established 1871.

R. R. Stratton	June 9, 1936 (appointed chairman May 21, 1941)
W. J. Brickley	February 3, 1937
A. G. Rice	June 1, 1938
F. R. Jouett	May 21, 1940
A. R. Gardner	May 21, 1941

COMMITTEE ON MEDICAL EDUCATION — Established 1881.

R. T. Monroe	May 21, 1941 (appointed chairman February 4, 1942)
G. D. Henderson	June 1, 1938
L. S. McKittrick	May 21, 1940
C. S. Keefer	February 4, 1942
I. R. Jankelson	May 25, 1942

COMMITTEE ON MEMBERSHIP — Established 1897.

H. F. Newton	June 9, 1931 (appointed chairman May 25, 1942)
John E. Fish	June 17, 1930
P. H. Leavitt	June 1, 1938
A. W. Reggio	May 21, 1940
L. S. McKittrick	May 25, 1942

COMMITTEE ON PUBLIC HEALTH — Established 1912.

F. P. Denny	June 1, 1938 (appointed chairman June 7, 1939)
Gerald Hoeffel	June 17, 1930
H. L. Lombard	June 4, 1935
H. F. Day	June 7, 1939
F. W. Marlow, Jr.	May 25, 1942

COMMITTEE ON MEDICAL DEFENSE — Established 1927.

A. W. Allen	June 7, 1927 (appointed chairman June 7, 1939)
E. D. Gardner	June 7, 1927
W. R. Morrison	June 9, 1936
(Sec. pro tem)	
Horatio Rogers	June 7, 1939
G. S. Reynolds	May 21, 1941

COMMITTEE ON SOCIETY HEADQUARTERS — Established 1932.

W. H. Robey	February 24, 1937 (chairman)
C. G. Mixter	June 8, 1932
J. M. Birnie	June 8, 1932
C. S. Butler	June 4, 1935
E. C. Miller	June 4, 1935

*Certain alternate members of the committee have not been chosen.

†Interim appointment.

COMMITTEE ON FINANCE — Established 1938

John Homans	June 2, 1938 (chairman)
E L. Hunt	June 2, 1938
C F Wilinsky	June 2, 1938
E J O'Brien, Jr	June 2, 1938
P P Johnson	October 4, 1939

COMMITTEE ON INDUSTRIAL HEALTH — Established 1942

Dwight O'Hara	May 25, 1942 (chairman)
J C Aub	May 25, 1942
D L Lynch	May 25, 1942
H C Marble	May 25, 1942
J C Merriam	May 25, 1942
T L. Shupman	May 25, 1942
J N Slurley	May 25, 1942

SPECIAL COMMITTEES

COMMITTEE ON CANCER — Established 1917

Shields Warren, Chairman, F G Balch, E M Daland,
P E Truesdale, C C Simmons

REPRESENTATIVES TO THE MASSACHUSETTS CENTRAL HEALTH COUNCIL

Barnstable W D Kinney
Berkshire R J Carpenter
Hampden G D Henderson
Norfolk F P Denny
Suffolk R B Osgood
Worcester E C Miller

COMMITTEE ON PUBLIC EDUCATION (a subcommittee of the Committee on Public Health) — Established 1930

F P Denny, *chairman*, Gerald Hoeffel *secretary*,
G R Minot, W H Robey, R M Smith, E H
Place, C C Simmons, J H Pratt, H W Stevens,
J B Ayer, H P Mosher, F R Ober, F P Joslin,
J D Barney, H L Lombard

COMMITTEE ON PUBLIC RELATIONS — Established 1931
(One counselor elected yearly by each district medical society, the president and president elect of the Society are chairman and vice-chairman respectively, and the vice president and secretary of the Society are members ex officio)

BARNSTABLE DISTRICT MEDICAL SOCIETY

W D Kinney, Osterville.

BERKSHIRE DISTRICT MEDICAL SOCIETY

P J Sullivan, Dalton, 471 Main Street

BRISTOL NORTH DISTRICT MEDICAL SOCIETY

J H Brewster, Attleboro, 178 South Main Street

BRISTOL SOUTH DISTRICT MEDICAL SOCIETY

H E Perry, New Bedford, 159 Cottage Street.

ESSEX NORTH DISTRICT MEDICAL SOCIETY

F S Bagnall, Groveland, 281 Main Street (Secretary of committee)

ESSEX SOUTH DISTRICT MEDICAL SOCIETY

E D Reynolds, Danvers, 48 High Street

FRANKLIN DISTRICT MEDICAL SOCIETY

H G Stetson, Greenfield, 39 Federal Street

HAMPODEN DISTRICT MEDICAL SOCIETY

P E Gear, Holyoke, 188 Chestnut Street

HAMPSHIRE DISTRICT MEDICAL SOCIETY

A J Bonnevill, Hatfield, 60 Main Street

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

J H Blaisdell, Winchester Office, Boston, 45 Bay
State Road

MIDDLESEX NORTH DISTRICT MEDICAL SOCIETY

D J Ellison, Lowell, 8 Merrimack Street

MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

J P Nelligan, Cambridge, 2336 Massachusetts Av-
enue

NORFOLK DISTRICT MEDICAL SOCIETY

N A Welch, West Roxbury Office, Boston, 520
Commonwealth Avenue

NORFOLK SOUTH DISTRICT MEDICAL SOCIETY

F A Bartlett, Wollaston, 308 Beale Street

PLYMOUTH DISTRICT MEDICAL SOCIETY

C D McCann, Brockton, 12 Cottage Street

SUFFOLK DISTRICT MEDICAL SOCIETY

A A Horner, Boston, 319 Longwood Avenue

WORCESTER DISTRICT MEDICAL SOCIETY

C A Sparrow, Worcester, 21 West Street

WORCESTER NORTH DISTRICT MEDICAL SOCIETY

J J Curley, Leominster, 82 Main Street

COMMITTEE ON POSTGRADUATE INSTRUCTION — Established 1932

Reginald Fitz, *chairman*, L E Parkins, *secretary*, J W
O'Connor, R N Nye, C J Kichham

COMMITTEE ON PHYSICAL THERAPY — Established 1935

F P Lowry, *chairman*, R B Osgood, G R Minot

COMMITTEE TO CONSIDER EXPERT TESTIMONY — Established 1936

F R Ober, *chairman*, David Cheever, F P McCar-
thy, Carl Bearse, W J Brickley *

COMMITTEE ON AUTOMOBILE INSURANCE CLAIMS — Estab-
lished 1937

H C Marble, *chairman*, H M Landesman, *secretary*,
P P Henson

COMMITTEE ON CONVALESCENT CARE — Established 1938

T D Jones, *chairman*, H E Gallup

COMMITTEE ON ARMY MEDICAL LIBRARY AND MUSEUM —
Established 1939

H R Viets, *chairman*, R B Osgood, Benjamin
Spector

COMMITTEE TO STUDY PRACTICE OF MEDICINE BY UNREGIS-
TERED PERSONS — Established 1939

Richard Dutton, *chairman*, B F Conley, E F Tim-
mins

*Interim appointment

TWENTY-FIVE VOTING MEMBERS IN THE MASSACHUSETTS HOSPITAL SERVICE, INC. — Established 1939.

B. H. Alton, E. S. Bagnall, G. M. Balboni, W. B. Breed, L. D. Chapin, H. F. Day, J. F. Donaldson, A. W. Dudley, John Fallon, J. E. Flynn, A. R. Gardner, H. W. Godfrey, D. L. Halbersleben, J. H. Lambert, A. A. Levi, Donald Monro,* A. E. Parkhurst, Helen S. Pitman, A. G. Rice, A. T. Ronan, F. W. Snow, G. L. Steele, R. R. Stratton,* J. E. Talbot, E. L. Young.

COMMITTEE CONCERNED WITH PREPAYMENT MEDICAL-CARE COSTS INSURANCE — Established 1940.

J. C. McCann, *chairman*; E. S. Bagnall, Shields Warren, P. H. Leavitt, W. B. Breed.

COMMITTEE ON TAX-SUPPORTED MEDICAL CARE — Established 1940.

E. S. Bagnall, *chairman*; A. L. Duncombe, A. A. Honor, E. L. Hunt, W. J. Pelletier.

COMMITTEE TO MEET WITH MASSACHUSETTS HOSPITAL ASSOCIATION — Established 1940.

W. G. Phippen, *chairman*; Frederic Hagler, G. S. Reynolds, E. D. Gardner, A. E. Parkhurst, F. W. Snow.

COMMITTEE TO EXAMINE WPA RECORDS — Established 1940.

G. L. Richardson, *chairman*; W. E. Browne, D. J. Ellison, L. R. Chaput, F. P. McCarthy.

COMMITTEE ON MATERNAL WELFARE — Established 1941.

J. A. Smith, *chairman*; Thomas Almy, R. L. DeNormandie, Eoline C. Dubois, C. J. Duncan, M. F. Eades, A. F. G. Edgelow, Flornece L. McKay, J. W. O'Connor, L. E. Phaneuf, G. M. Shipton, W. R. Sisson, R. M. Smith, R. S. Titus, R. J. Williams.

COMMITTEE TO STUDY THE PRACTICE OF MEDICINE — Established 1941.

Dwight O'Hara, *chairman*; B. H. Alton, A. E. Parkhurst, D. D. Scannell, Conrad Wesselhoeft.

COMMITTEE ON REHABILITATION — Established 1941.

W. E. Browne, *chairman*; W. M. Collins, J. J. Regan, B. F. Andrews, R. M. Chambers, A. L. Watkins, John Fallon.*

COMMITTEE CONCERNED WITH POSTPAYMENT MEDICAL-CARE COSTS THROUGH BANKS — Established 1942.

E. S. Bagnall, *chairman*; H. G. Stetson, D. J. Ellison.

COMMITTEE OF ONE TO VISIT VARIOUS STATE-AIDED CANCER CLINICS FOR PURPOSE OF REPORTING TO SOCIETY THEIR PRESENT STATE — Established 1942.

C. C. Simmons.

COMMITTEE ON LEGISLATION — Established 1942. (One councilor elected yearly by each district medical society.)

BARNSTABLE DISTRICT MEDICAL SOCIETY — Not yet elected.

BERKSHIRE DISTRICT MEDICAL SOCIETY — Not yet elected.

BRISTOL NORTH DISTRICT MEDICAL SOCIETY — J. L. Murphy, Taunton, 23 Cedar Street.

BRISTOL SOUTH DISTRICT MEDICAL SOCIETY — Not yet elected.

ESSEX NORTH DISTRICT MEDICAL SOCIETY — E. H. Ganley, Methuen, 251 Broadway.

ESSEX SOUTH DISTRICT MEDICAL SOCIETY — C. A. Worthen, Lynn, 19 Park Street.

FRANKLIN DISTRICT MEDICAL SOCIETY — Not yet elected.

HAMPDEN DISTRICT MEDICAL SOCIETY — Not yet elected.

HAMPSHIRE DISTRICT MEDICAL SOCIETY — Not yet elected.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY — K. L. MacLachlan, Melrose, 1 Bellevue Avenue.

MIDDLESEX NORTH DISTRICT MEDICAL SOCIETY — Not yet elected.

MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY — Not yet elected.

NORFOLK DISTRICT MEDICAL SOCIETY — Not yet elected.

NORFOLK SOUTH DISTRICT MEDICAL SOCIETY — Not yet elected.

PLYMOUTH DISTRICT MEDICAL SOCIETY — Not yet elected.

SUFFOLK DISTRICT MEDICAL SOCIETY — W. B. Breed, Boston, 264 Beacon Street.

WORCESTER DISTRICT MEDICAL SOCIETY — Not yet elected.

WORCESTER NORTH DISTRICT MEDICAL SOCIETY — Not yet elected.

COMMITTEE ON BOSTON MEDICAL LIBRARY — Established 1942.

W. H. Robey,* *chairman*; C. S. Butler,* David Cheever,* M. A. Tighe,* Shields Warren.*

REPRESENTATIVE TO MENTAL HEALTH FOR DEFENSE ORGANIZATION.

Abraham Myerson.

REPRESENTATIVE TO THE HOSPITAL COUNCIL OF BOSTON FOR THE YEAR 1942.

Fletcher H. Colby.

DELEGATES AND ALTERNATES TO THE HOUSE OF DELEGATES, AMERICAN MEDICAL ASSOCIATION FOR 1942-1943

Delegates

Alternates

June 1, 1941 to June 1, 1943

J. M. Birnie, Springfield	R. J. Carpenter, Pittsfield
R. H. Miller, Boston	Cadis Phipps, Brookline

June 1, 1942 to June 1, 1944

D. D. Scannell, Jamaica Plain	E. S. Bagnall, Groveland
Dwight O'Hara, Waltham	E. L. Hunt, Worcester
C. E. Mongan, Somerville	C. J. Kickham, Brookline
W. G. Phippen, Salem	J. I. B. Vail, Hyannis

MASSACHUSETTS COMMITTEE OF PROCUREMENT AND ASSIGNMENT SERVICE† — Established 1942

Reginald Fitz, *chairman*; H. M. Clute, J. J. Curley, E. L. Kickham, Dwight O'Hara, W. H. Pulsifer

*Interim appointment.

†This is not a committee of the Massachusetts Medical Society. It is here listed for purposes of information only.

COUNCILORS FOR 1942-1943

ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR
ANNUAL MEETINGS, APRIL 15 TO MAY 15, 1942

BARNSTABLE

J G Kelley, Pocasset, Barnstable County Sanatorium,
V P
J L Chute, Osterville, A M N C
D E Higgins, Cotuit, Mun St, Sec
C H Keene, Chatham, Seaview St
W D Kinney, Osterville, E C, M N C

BERKSHIRE

G M Shipton, Pittsfield, 74 North St, V P
J J Boland, Pittsfield, 334 North St, E C
T F Crowley, North Adams, 247 Eagle St
I S F Dodd, Pittsfield, 34 Fenn St
C F Tasce, Pittsfield, 311 North St, A M N C
E A Kennedy, Pittsfield, 100 North St
G S Reynolds, Pittsfield, 7 North St, Sec
Solomon Schwager, Pittsfield, 246 North St
P J Sullivan, Dalton, 471 Main St, M N C

BRISTOL NORTH

J A Reese, Attleboro, 48 Bank St, V P
W H Allen, Mansfield, 70 North Main St, F C,
M N C
J H Brewster, Attleboro, 178 South Mun St
R M Chambers, Taunton, Taunton State Hospital,
A E C
J L Murphy, Taunton, 23 Cedar St, A M N C
W H Swift, Taunton, 141 High St, Sec

BRISTOL SOUTH

C A Bonney, Jr, New Bedford, 41 Maple St, V P
G W Blood, Fall River, 82 New Boston Rd
R B Butler, Fall River, 278 North Main St, A M
N C
F F Cody, New Bedford, 105 South Sixth St, M N C
J A Fournier, Fall River, 11 Choate St
E D Gardner, New Bedford, 150 Cottage St, E C
F M Howes, New Bedford, 135 Cottage St
D R Mills, Edgartown
H E Perry, New Bedford, 159 Cottage St
A H Sterns, New Bedford, 31 Seventh St, Sec
I N Tilden, Mattapoisett, Barstow St
C C Tripp, New Bedford, 416 County St
P E Truesdale, Fall River, 151 Rock St

ESSEX NORTH

E S Bagnall, Groveland, 281 Main St, V P
R V Baketel, Methuen, 7 Hampshire St
L R Chaput, Haverhill, 3 Washington Sq
J P Creed, Haverhill, 112 Emerson St
E H Ganley, Methuen, 251 Broadway
H R Kurth, Lawrence, 57 Jackson St, Sec
P J Look, Andover, 115 Main St
R C Norris, Methuen, 247 Broadway, A E C, A M
N C
G L Richardson, Haverhill, 94 Emerson St, M N C
F W Snow, Newburyport, 24 Essex St, E C
D W Wallwork, North Andover, 5 Third St
C F Warren, Amesbury, 1 School St

ESSEX SOUTH

D S Clark, Salem, 2 Oliver St, V P
Bernard Appel, Lynn, 281 Ocean St, M N C
H A Boyle, Middleton, Essex Sanatorium

C P Brown, Swampscott, 74 Humphrey St
Hanford Carvel, Gloucester, 1033 Washington St
C L Curtis, Salem, 10 Federal St, A E C
R C Foss, Peabody, 125 Main St
Loring Grimes, Swampscott, 84 Humphrey St, E C
P P Johnson, Beverly, 1 Monument Sq, A M N C
B B Mansfield, Ipswich, 4 Green St
A E Parkhurst, Beverly, Monument Sq
O S Pettingill, Middleton, Essex Sanatorium
W G Phippen, Salem, 31 Chestnut St, Ex Pres
H G Pope, Swampscott, 90 Humphrey St, Sec.
J D Reynolds, Danvers, 48 High St
E R Shaugnessy, Salem, 24½ Winter St
J W Trask, East Lynn, 90 Ocean St
C F Twomey, East Lynn, 80 Ocean St
C A Worthen, Lynn, 19 Park St

FRANKLIN

A W Hayes, Greenfield, 78 Federal St, V P
F J Barnard, Greenfield, 479 Main St, E C, M N C
H L Craft, Ashfield, Sec
A H Ellis, Greenfield, 58 Federal St
W J Pelletier, Turners Falls, 113 Ave. A, A M
N C
H G Stetson, Greenfield, 39 Federal St, Ex Pres

HAMPTDEN

G L Steele, Springfield, 20 Maple St, V P, E C
F H Allen, Holyoke, 16 Fairfield St
E P Bagg, Holyoke, 207 Elm St
W C Barnes, Springfield, 146 Chestnut St, Sec.
J M Birnie, Springfield, 146 Chestnut St, Ex Pres
H F Byrnes, Springfield, 6 Chestnut St
W A R Chapin, Springfield, 121 Chestnut St
J L Chereskin, Springfield, 333 Bridge St
G B Corcoran, West Springfield, 84 Park St
A J Douglas, Westfield, 93 Elm St
E C Dubois, Springfield, 174 Buckingham St
Adolph Franz, Jr, Holyoke, 276 Maple St
G L Gabler, Holyoke, 4 Bullard Ave
P E Gear, Holyoke, 188 Chestnut St
Frederic Hagler, Springfield, 20 Maple St
G D Henderson, Holyoke, 312 Maple St
Charles Jurist, Springfield, 70 Chestnut St
L A Knowlton, Holyoke, 207 Elm St, A M N C
O J Menard, Springfield, 146 Chestnut St
M W Pearson, Ware, 19 Pleasant St
A G Rice, Springfield, 146 Chestnut St, M N C
G L Schadt, Springfield, 44 Chestnut St, President

HAMPSHIRE

Mary P Snook, Chesterfield, V P
A J Bonnevill, Hatfield, 60 Main St
R S Clapp, Amherst, 110 North Pleasant St
J D Collins, Northampton, 187 Main St, A M N C
J R Hobbs, Williamsburg, Main St, Sec.
L B Pond, Easthampton, 115 Main St, E C, M N C

MIDDLESEX EAST

C W De Wolf, Melrose, 8 Porter St, V P
J H Blusdell, Winchester, Office Boston, 45 Bay
State Rd
Richard Dutton, Wakefield, 33 Avon St, A E C
E M Halligan, Reading, 37 Salem St, A M N C
J H Kerrigan, Stoneham, 481 Main St
K L MacLachlan, Melrose, 1 Bellevue Ave, Sec, F C
M J Quinn, Winchester, 44 Church St

*Interim appointment

R. R. Stratton, Melrose, 538 Lynn Fells Parkway,
M. N. C., C.
J. M. Wilcox, Woburn, 6 Bennett St.

MIDDLESEX NORTH

M. A. Tighe, Lowell, 9 Central St., Secretary, V. P.
M. L. Alling, Lowell, 9 Central St.
H. R. Coburn, Lowell, 202 Merrimack St.
W. M. Collins, Lowell, 174 Central St., E. C.
R. L. Drapeau, Lowell, 174 Central St., Sec.
D. J. Ellison, Lowell, 8 Merrimack St.
A. R. Gardner, Lowell, 16 Shattuck St., A. M. N. C.
W. F. Ryan, Lowell, 219 Central St.
W. H. Sherman, Lowell, 9 Central St., M. N. C.

MIDDLESEX SOUTH

H. F. Day, Cambridge, 34 Kirkland St., V. P.
C. F. Atwood, Arlington, 821 Massachusetts Ave.
E. W. Barron, Malden, Office Boston, 20 Ash St.
W. B. Bartlett, Concord, 28 Monument St.
Harris Bass, Everett, 351 Broadway.
J. M. Baty, Belmont, Office Brookline, 1101 Beacon St.
S. M. Biddle, Cambridge, 206 Huron Ave.
E. H. Bigelow, Framingham, Hotel Kendall, Ex-Pres.
W. O. Blanchard, Newton, 465 Centre St.
G. F. H. Bowers, Newton Highlands, 156 Woodward St.
R. W. Buck, Waban, Office Boston, 5 Bay State Rd.
E. J. Butler, Cambridge, 25 Garden St.
J. J. Cochran, Natick, 15 W. Central St.
B. F. Conley, Malden, 51 Main St.
C. L. Derick, Newton Highlands, Office Boston, 412 Beacon St.
J. G. Downing, Newton, Office Boston, 520 Commonwealth Ave.
C. W. Finnerty, West Somerville, 5 Pearson Rd.
H. Q. Gallupe, Waltham, 751 Main St.
F. W. Gay, Malden, 20 Park St.
H. G. Giddings, Newton Centre, Office Boston, 270 Commonwealth Ave.
H. W. Godfrey, Auburndale, 14 Hancock St.
A. D. Guthrie, Medford, 408 Salem St.
R. D. Halloran, Waltham, Metropolitan State Hospital.
Eliot Hubbard, Jr., Cambridge, 29 Highland St., Assistant Treasurer.
L. H. Jack, West Newton, 379 Austin St.
A. M. Jackson, Everett, 512 Broadway.
E. E. Kattwinkel, West Newton, 65 Sterling St.
W. N. Lanigan, Medford, 187 Main St.
A. A. Levi, Newton, Office Boston, 481 Beacon St., Sec.
F. P. Lowry, Newton, 313 Washington St.
A. N. Makechnie, Cambridge, 14 Upland Rd.
R. A. McCarty, Waltham, 751 Main St.
J. C. Merriam, Framingham, 198 Union Ave., A. M. N. C.
Dudley Merrill, Cambridge, 51 Brattle St.
C. E. Mongan, Somerville, 24 Central St., Ex-Pres.
G. M. Morrison, Waban, Office Boston, 520 Commonwealth Ave., C.
J. P. Nelligan, Cambridge, 2336 Massachusetts Ave.
S. J. G. Nowak, Belmont, Office Boston, Boston City Hospital.
E. J. O'Brien, Jr., Newton, Office Boston, 270 Commonwealth Ave.
Dwight O'Hara, Waltham, Office Boston, 5 Bay State Rd., M. N. C., C.
L. G. Paul, Newton Centre, Office Boston, 270 Commonwealth Ave.

Max Ritvo, Newton, Office Boston, 485 Commonwealth Ave.

E. H. Robbins, Somerville, 334 Broadway.
E. S. A. Robinson, Newton Centre, Office Jamaica Plain, 375 South St.
W. D. Roche, Marlboro, 196 Main St.
E. F. Ryan, Maynard, 74 Main St.
M. J. Schlesinger, Newton, Office Boston, 330 Brookline Ave.
J. W. Sever, Cambridge, Office Boston, 321 Dartmouth St.
E. F. Sewall, Somerville, 380 Broadway.
E. W. Small, Belmont, 68 Leonard St.
H. W. Thayer, Newtonville, 355 Walnut St.
A. B. Toppan, Watertown, 289 Mt. Auburn St.
J. E. Vance, Natick, Office Boston, 510 Commonwealth Ave.
B. M. Wein, Newton, Office Boston, 471 Commonwealth Ave.
R. H. Wells, Lexington, 1430 Massachusetts Ave.
M. W. White, Somerville, 21 Walnut St.
Alfred Worcester, Waltham, 314 Bacon St., Ex-Pres.
Hovhannes Zovickian, Watertown, 528 Mt. Auburn St.

NORFOLK

J. A. Seth, Milton, Office Boston, 47 Bay State Rd., V. P.
J. R. Barry, West Roxbury, 1857 Centre St.
Carl Bearse, Boston, 483 Beacon St., E. C.
Arthur Berk, Brookline, Office Boston, 270 Commonwealth Ave.
M. I. Berman, Dorchester, 1071A Blue Hill Ave.
G. F. Blood, Roslindale, 20 Belgrade Ave.
L. F. Curran, Dorchester, Office Boston, 409 Marlboro St.
William Dameshek, Brookline, Office Boston, 371 Commonwealth Ave.
F. P. Denny, Brookline, 111 High St., C.
Albert Ehrenfried, Brookline, Office Boston, 520 Beacon St.
J. J. Elliott, Roslindale, 4258 Washington St.
H. M. Emmons, Needham, Office Boston, 354 Commonwealth Ave.
J. E. Fish, Canton, Massachusetts Hospital School.
J. C. V. Fisher, West Roxbury, Office Boston, 510 Commonwealth Ave.
Morris Frank, Roxbury, 173 Humboldt Ave.
Susannah Friedman, Roxbury, Office Boston, 485 Commonwealth Ave.
David Glunts, Roxbury, 2 Franklin Garden.
B. T. Guild, Dorchester, Office Boston, 475 Commonwealth Ave.
D. L. Halbersleben, Brookline, Office Roslindale, 818 South St.
J. B. Hall, Roxbury, 60 Windsor St.
R. J. Heffernan, Jamaica Plain, Office Brookline, 1101 Beacon St.
H. J. Inglis, Chestnut Hill, Office Boston, 43 Bay State Rd., A. M. N. C.
I. R. Jankelson, Jamaica Plain, Office Boston, 483 Beacon St.
H. L. Johnson, West Roxbury, Office Boston, 520 Commonwealth Ave.
C. J. Kickham, Brookline, Office Boston, 524 Commonwealth Ave.
C. J. E. Kickham, Jamaica Plain, Office Boston, 12 Bay State Rd.
E. L. Kickham, Brookline, Office Boston, 270 Commonwealth Ave.

D L. Lionberger, Dedham, Office Roslindale, 3 Con-
way St
D S Luce, Canton, 553 Washington St
C M Lyon, Dorchester, 276 Bowdoin St
D L Lynch, Roslindale, Office Boston, 245 State St
T F P Lyons, Milton, Office Boston, 270 Common-
wealth Ave, Sec
Charles Malone, Jamaica Plain, 46 St John St
F P McCarthy, Milton, Office Boston, 371 Common-
wealth Ave
R T Monroe, Brookline, Office Boston, 270 Common-
wealth Ave, C
F J Moran, Dedham, 395 Washington St
Hyman Morrison, Roxbury, Office Boston, 493 Beacon
St
M W O'Connell, West Roxbury, Office Boston Boston
City Hospital
H C Peterson, West Roxbury, Office Boston 29 Bay
State Rd
Frederick Reis, Jamaica Plain, Office Boston, 416 Hunt-
ington Ave
S A Robins, Roxbury, Office Boston 636 Beacon St
S M Saltz, Roxbury, 294 Seaver St
D D Scannell, Jamaica Plain, Office Boston, 475 Com-
monwealth Ave, M N C
Kathlyne S Snow, Jamaica Plain, Office Boston, 466
Commonwealth Ave
J W Spellman, Milton, Office Brookline, 1101 Beacon
St
M H Spellman, Jamaica Plain, Office Boston, 475
Commonwealth Ave
J P Treanor, Jr, Jamaica Plain, Office Brookline,
1101 Beacon St
W J Walton, Dorchester, 106 Bowdoin St
N A Welch, West Roxbury, Office Boston, 520 Com-
monwealth Ave

NORFOLK SOUTH

W L Sargent, Quincy, 24 Whitney Rd, V P
C S Adams, Wollaston, 62 Brooks St
F A Bartlett, Wollaston, 308 Beale St
H H A Blyth, Quincy, 24 Russell Park, Sec.
R L Cook, Quincy, 38 Russell Park
F W Crawford, Holbrook, 98 North Franklin St
J E Knowlton, Quincy, 579 Hancock St
L W Pease, Weymouth, 135 Webb St
D B Reardon, Quincy, 1186 Hancock St, E C,
M N C
H A Robinson, Hingham, 205 North St, A M N C

PLYMOUTH

C D McCann, Brockton, 12 Cottage St, V P
J E Brady, Brockton, 231 Main St
Charles Hammond, Hanover, Washington St
W T Hanson, State Farm
P B Kelly, Plymouth, 27 Court St
P H Leavitt, Brockton, 129 West Elm St, Vice
President, E C, A M N C
R C McLeod, Brockton, Goddard Hospital, Sec
G A Moore, Brockton, 167 Newbury St, A C C
D W Pope, Brockton, 12 Cottage St
W H Pulsifer, Whitman, 26 Park Ave, M N C

SUFFOLK

J P O'Hare, Boston, 520 Commonwealth Ave, V P
H L Albright, Boston, 412 Beacon St, Sec
A W Allen, Boston, 264 Beacon St, C
J W Bartol, Boston, 1 Chestnut St, Ex Pres
H L Blumgart, Boston, 330 Brookline Ave

W B Breed, Boston, 264 Beacon St, M N C
W J Brickley, Boston, 524 Commonwealth Ave
W E Browne, Boston, 587 Beacon St
C S Butler, Boston, 257 Newbury St, Treasurer
G C Cramer, Boston, 63 Marlboro St
E M Chapman, Boston, 270 Commonwealth Ave
David Cheever, Boston, 193 Marlboro St
H M Clute, Boston, 171 Bay State Rd
Pasquale Costanza, East Boston, 238 Maverick St
R L DeNormandie, Boston, 330 Dartmouth St
N W Faxon, Boston, Massachusetts General Hospital
G B Fenwick, Chelsea, 38 Cary Ave
Reginald Fitz, Boston 319 Longwood Ave
Maurice Fremont Smith, Boston, 12 Hereford St
Channing Frothingham, Boston, Office Jamaica Plain,
1153 Centre St, Ex Pres
M N Fulton, Brookline, 1101 Beacon St
Joseph Garland, Boston, 266 Beacon St
John Homars, Boston, 311 Beacon St, C
A A Hornor, Boston 319 Longwood Ave, A M N C
L M Hurvath, Boston, 605 Commonwealth Ave
C S Keefer, Boston, 78 East Concord St
H A Kelly, Winthrop, 200 Pleasant St
R I Lee, Boston, 264 Beacon St, President Elect
C C Lund, Boston, 319 Longwood Ave A E C
W J Mixer, Boston, 319 Longwood Ave
Donald Munro, Boston, 818 Harrison Ave E C
H L Musgrave Revere, 622 Beach St
H F Newton, Boston, 319 Longwood Ave, C
R N Nye, Boston, 8 Fenway
F R Ober, Boston, 234 Marlboro St, Ex Pres
L E Parkins, Boston, 12 Bay State Rd
L E Phineuf, Boston, 270 Commonwealth Ave
Helen S Pittman, Boston 412 Beacon St
W H Robey, Boston, 202 Commonwealth Ave, Ex
Pres, C
G C Shattuck, Boston, 25 Shattuck St
R M Smith Boston 66 Commonwealth Ave, C
E F Timmins, South Boston, 527 Broadway
S N Vose Boston, 29 Bay State Rd
Shields Warren, Boston, 195 Pilgrim Rd
Conrad Wesselhoeft, Boston, 315 Marlboro St
C F Wilinsky, Boston, 330 Brookline Ave

WORCESTER

Gordon Berry, Worcester, 36 Pleasant St, V P
J I Ashkins, Milford, 36 Pine St
J C Austin, Spencer, 176 Main St
W P Bowers, Clinton, 264 Chestnut St, Ex Pres
L R Bragg, Webster, 260 Main St
P H Cook, Worcester, 27 Elm St
G A Dix, Worcester, 6 Ashland St
E B Emerson, Rutland, Rutland State Sanatorium
J M Fallon, Worcester, 390 Main St
L M Felton, Worcester, 36 Pleasant St
E L Hunt, Worcester, 28 Pleasant St
E R Leib, Worcester, 36 Pleasant St
W F Lynch, Worcester, 390 Main St, A M N C
J C McCann, Worcester, 390 Main St
J M Melick, Worcester, 27 Elm St
A E O'Connell, Worcester, 390 Main St
J W O'Connor, Worcester, 36 Pleasant St
R S Perkins, Worcester, 10 Hackfield Rd, E C
W C Seelye, Worcester, 390 Main St
C A Sparrow, Worcester, 21 West St
J J Tegelberg, Worcester, 390 Main St, Sec
G C Tully, Worcester, 34 Elm St

*Interim appointment

R. J. Ward, Worcester, 9 Bellevue St.
 F. H. Washburn, Holden, Holden Clinic.
 R. P. Watkins, Worcester, 332 Main St., M. N. C.
 S. B. Woodward, Worcester, 58 Pearl St., Ex-Pres.

WORCESTER NORTH

H. C. Arey, Gardner, 66 Parker St., V. P.
 E. A. Adams, Fitchburg, 40 Oliver St., Sec.
 J. J. Curley, Leominster, 82 Main St., E. C.
 C. B. Gay, Fitchburg, 62 Day St., A. M. N. C.
 J. C. Hales, Gardner, 66 Parker St.
 G. P. Keaveny, Fitchburg, 62 Fox St.
 B. P. Sweeney, Leominster, 5 Gardner Place, M. N. C.

The initials E. C. following the name of a councilor indicate that he is a member of the Executive Committee, and A. E. C. that he is an alternate member of the Executive Committee, M. N. C. that he is a member of the Committee on Nominations and A. M. N. C. that he is an alternate member of the Committee on Nominations; V. P. that a member is a councilor by virtue of his office as president of a district society and so vice-president of the general society, C. by virtue of his office as chairman of a standing committee, Sec. by virtue of his office as secretary of a district society and Ex-Pres. by virtue of being a past president.

CENSORS FOR 1942-1943

BARNSTABLE

W. D. Kinney, Osterville, *supervisor*.
 E. F. Curry, Sagamore.
 C. E. Harris, Hyannis.
 J. L. Chute, Osterville.
 J. I. B. Vail, Hyannis.

BERKSHIRE

I. S. F. Dodd, Pittsfield, *supervisor*.
 M. T. Cavanaugh, Great Barrington.
 W. T. Frawley, Pittsfield.
 N. B. McWilliams, Williamstown.
 F. R. Smith, Pittsfield.

BRISTOL NORTH

W. H. Allen, Mansfield, *supervisor*.
 W. H. Bennett, Taunton.
 C. B. Kingsbury, Taunton.
 L. E. Butler, Taunton.
 H. L. Rich, Attleboro.

BRISTOL SOUTH

F. M. Howes, New Bedford, *supervisor*.
 W. F. MacKnight, Fall River.
 E. A. McCarthy, Fall River.
 Henry Wardle, Fall River.
 C. C. Persons, New Bedford.

ESSEX NORTH

R. V. Baketel, Methuen, *supervisor*.
 L. C. Peirce, Newburyport.
 F. A. O'Reilly, Lawrence.
 E. M. Gale, Merrimac.
 A. P. George, Haverhill.

ESSEX SOUTH

A. E. Parkhurst, Beverly, *supervisor*.
 J. G. Adams, Salem.
 W. C. Inman, Danvers.
 I. B. Hull, Gloucester.
 C. A. Worthen, Lynn.

FRANKLIN

W. J. Pelletier, Turners Falls, *supervisor*.
 A. H. Wright, Northfield.
 J. E. Moran, Greenfield.
 H. M. Kemp, Greenfield.
 P. N. Freeman, Greenfield.

HAMPDEN

Frederic Hagler, Springfield, *supervisor*.
 G. F. Dalton, Springfield.
 W. J. Dillon, Springfield.
 P. M. Moriarty, Chicopee.
 J. B. Bigelow, Holyoke.

HAMPSHIRE

A. J. Bonneville, Hatfield, *supervisor*.
 M. E. Cooney, Northampton.
 T. F. Corriden, Northampton.
 J. E. Hayes, Northampton.
 C. H. Wheeler, Haydenville.

MIDDLESEX EAST

M. J. Quinn, Winchester, *supervisor*.
 C. E. Montague, Wakefield.
 J. H. Fay, Melrose.
 S. H. Moses, Winchester.
 J. L. Anderson, Reading.

MIDDLESEX NORTH

M. L. Alling, Lowell, *supervisor*.
 F. R. Brady, Lowell.
 R. C. Stewart, Lowell.
 H. L. Leland, Lowell.
 J. J. Cassidy, Lowell.

MIDDLESEX SOUTH

H. Q. Gallupe, Waltham, *supervisor*.
 C. W. Finnerty, West Somerville.
 J. E. Vance, Natick.
 A. N. Makechnie, Cambridge.
 H. W. Thayer, Newtonville.

NORFOLK

Hyman Morrison, Roxbury, *supervisor*.
 D. L. Lionberger, Dedham.
 B. E. Sibley, Brookline.
 Marjorie Woodman, Jamaica Plain.
 C. E. Allard, Dorchester.

NORFOLK SOUTH

C. S. Adams, Wollaston, *supervisor*.
 H. A. Robinson, Hingham.
 D. L. Belding, Hingham.
 C. J. Lynch, Quincy.
 D. J. Bailey, Weymouth.

PLYMOUTH

W. T. Hanson, State Farm, *supervisor*.
 J. H. Dunn, Rockland.
 G. A. Buckley, Brockton.
 B. H. Peirce, South Hanson.
 A. W. Carr, Bridgewater.

SUFFOLK

Donald Munro, Boston, *supervisor*.
 A. J. A. Campbell, Boston.
 J. H. Pratt, Boston.
 F. D. Adams, Boston.
 A. W. Reggio, Boston.

WORCESTER

G A Dix, Worcester, *supervisor*
 B C Wheeler, Worcester
 S M Gibson, Southbridge.
 D G Ljungberg, Worcester
 J T Brosnan, Worcester

WORCESTER NORTH

C B Gay, Fitchburg, *supervisor*
 F J Djerf, Fitchburg
 G P Keaveny, Fitchburg
 F A Reynolds, Athol
 J A McLean, Ayer

VICE PRESIDENTS OF THE MASSACHUSETTS MEDICAL SOCIETY (*Ex Officio*)

FOR 1942-1943

PRESIDENTS OF DISTRICT MEDICAL SOCIETIES

(Arranged according to seniority of fellowship
in the Massachusetts Medical Society)

BRISTOL SOUTH — C A Bonney, Jr, New Bedford
 NORFOLK SOUTH — W L Sargent, Quincy
 MIDDLESEX SOUTH — H F Day, Cambridge
 WORCESTER — Gordon Berry, Worcester
 MIDDLESEX NORTH — Michael A Tighe, Lowell
 BRISTOL NORTH — J A Reese, Attleboro
 PLYMOUTH — C D McCann, Brockton
 MIDDLESEX EAST — W DeWolf, Wakefield
 SUFFOLK — J P O'Hare, Boston
 WORCESTER NORTH — H C Arey, Gardner
 ESSEX NORTH — E S Bagnall, Groveland
 HAMPSHIRE — G L Steele, Springfield
 ESSEX SOUTH — D S Clark, Salem
 BERKSHIRE — G M Shipton, Pittsfield
 HAMPSHIRE — Mary P Snook, Chesterfield
 NORFOLK — J A Seth, Dorchester
 FRANKLIN — A W Hayes, Greenfield
 BARNSTABLE — J G Kelley, Pocasset

COMMISSIONERS OF TRIAL FOR 1942-1943

BARNSTABLE — F O Cass, Provincetown
 BERKSHIRE — I S F Dodd, Pittsfield
 BRISTOL NORTH — J W Cook, Mansfield
 BRISTOL SOUTH — A C Lewis, Fall River
 ESSEX NORTH — F W Anthony, Haverhill
 ESSEX SOUTH — O C Blair, Lynn
 FRANKLIN — K W D Jacobus, Turners Falls
 HAMPSHIRE — J M Pirnie, Springfield
 HAMPSHIRE — E H Copeland, Northampton
 MIDDLESEX EAST — T E Caulfield, Jr, Woburn
 MIDDLESEX NORTH — J F Boyle, Lowell
 MIDDLESEX SOUTH — H P Stevens, Cambridge
 NORFOLK — W J Walton, Dorchester
 NORFOLK SOUTH — F A Bartlett, Wollaston
 PLYMOUTH — J A Carluccio, Brockton
 SUFFOLK — J R Torbert, Boston
 WORCESTER — W P Bowers, Clinton
 WORCESTER NORTH — J C Hales, Gardner

OFFICERS OF THE SECTIONS FOR 1943

ELECTED BY THE SECTIONS

(The street addresses may be obtained from the
Directory of Officers and Fellows)

SECTION OF MEDICINE

Chairman, Laurence D Chappin, Springfield *secretary*,
Richard P Stetson, Chestnut Hill

SECTION OF SURGERY

Chairman, James C McCann, Worcester *secretary*,
Oliver Cope, Cambridge *Executive Committee* —
Ernest M Daland, Newton and Boston (1 year),
Archibald M Fraser, Boston (2 years), Stanley J G
Nowak, Belmont and Boston (3 years)

SECTION OF PEDIATRICS

Chairman, James Marvin Baty, Belmont and Brookline
secretary, Gerald Hoeffel, Cambridge

SECTION OF OBSTETRICS AND GYNECOLOGY

Chairman, Christopher J Duncan, Waban, *vice-chair*
man, Arthur F G Edgewood, Springfield *secretary*,
George Van S Smith, Brookline

SECTION OF RADIOLOGY

Chairman, Joseph H Marks, Newton *secretary*, Stan-
ley A Wilson, Marblehead

SECTION OF PHYSIOTHERAPY

Chairman, Henry A Tadgell, Winchester *secretary*,
Wilmot L Marden, Lynn

SECTION OF DERMATOLOGY AND SYPHILOLOGY

Chairman, J Harper Blissell, Winchester, *secretary*,
G Marshall Crawford, Lincoln

OFFICERS OF THE DISTRICT MEDICAL SOCIETIES FOR 1942-1943

ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR
ANNUAL MEETINGS IN 1942

(The street addresses may be obtained from the
Directory of Officers and Fellows)

BARNSTABLE — *President*, Julius G Kelley, Pocasset
vice president, Joseph N Kelly, Orleans, *secretary*, Donald
E Higgins, Cotuit *treasurer*, Harold F Rowley, Harwich
Port, *librarian*, Carroll H Keene, Chatham *executive*
councilor, William D Kinney, Osterville

BERKSHIRE — *President*, George M Shipton, Pittsfield
vice president, Charles T Leslie, Pittsfield, *secretary*,
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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, MD, *Editor*

CASE 28281

PRESENTATION OF CASE

A fifteen-year-old schoolboy was admitted to the hospital because of weakness following an illness characterized by jaundice and skin eruption.

The patient was well until a year before entry, when there was insidious onset of slight jaundice, accompanied by and possibly slightly preceded by lack of energy. The stools and urine both appeared light yellow. The patient was advised by his physician to take a dose of "salts" nightly. Subsequently, hemorrhoids developed and required lancing. However, the jaundice persisted, and was accompanied by yellow urine and stools, moderate anorexia and lassitude. Nine months before entry, blisters filled with yellowish, watery fluid appeared on the front of the chest. His physician prescribed a paste and a lotion, which somewhat allayed the itching. The lesions spread to the posterior surfaces of the legs and thighs. A dermatologist prescribed vitamin D and sodium cacodylate. The latter drug was given intramuscularly in 3 gr. doses, daily at first and later every other day. The blisters "turned purple" and then dried up. In a month, the patient's skin was clear. Therapy was discontinued, and in ten days the entire surface of the back and the inner aspects of the thighs were involved by a severe recurrence. The blisters were as large as "bunches of grapes." Cacodylate therapy was reinstituted, with improvement as dramatic as before. Throughout the nine months preceding entry, the patient's slight jaundice remained unaltered. There was some improvement in appetite. The colors of the urines and stools tended to fluctuate, with an inverse relation, one becoming lighter as the other darkened. Two weeks before entry, the patient developed a sore throat, with swelling of the lymph nodes in the right side of the neck, fever and darkening of the urine. There was also some swelling of the abdomen. Fifteen pounds' weight was lost in the first six months of the illness, and regained in the last six months.

The past and family histories were essentially irrelevant. A maternal aunt had hives. There was no known exposure to fumes or gases, and no drugs were taken other than those prescribed in the course of the illness. Tetanus antiserum

was given to the patient three years before entry, when a firecracker exploded in his hand.

On admission, the patient appeared well developed and nourished. There was marked icterus of the scleras and of the warm, dry skin. The mouth and throat were dry and injected, with ragged, badly infected tonsils. Several teeth were carious. The posterior auricular and cervical lymph nodes were slightly enlarged, as were the nodes in the axillas and groins. The heart was of normal size, but seemed pushed upward. There was a soft apical systolic murmur. The lungs were clear. The abdomen was slightly distended, with bulging in the flanks and shifting dullness, although a fluid wave could not be elicited. The spleen was considerably enlarged, although not easily palpable. The liver seemed of normal size.

The blood pressure was 136 systolic, 76 diastolic. The temperature was 103°F, the pulse 100, and the respirations 22.

Examination of the blood showed a red cell count of 3,710,000 with 10 gm hemoglobin, and a white cell count of 4700 with 47 per cent polymorphonuclears (including 13 per cent band forms), 36 per cent large lymphocytes, 9 per cent small lymphocytes, 7 per cent monocytes and 1 per cent eosinophils. The hematocrit was 35 per cent. There were 15 per cent reticulocytes. The prothrombin time was prolonged to about twice normal. There was no increase in red cell fragility. The van den Bergh reaction was biphasic, at 90 mg per 100 cc. The serum albumin was 2.13 gm, and the globulin 4.99 gm per 100 cc. The nonprotein nitrogen was normal, with a reduction in urea nitrogen. The formal gel test was positive. Agglutination tests for heterophil antigen were negative. Four blood cultures were negative. The urine showed a + test for albumin, a trace of sugar and a ++ test for bile pigment, and was urobilinogen positive in a dilution of 1:20. The stools were gelatinous and yellow, with a negative guaiac reaction, culture was negative for pathogenic organisms.

A roentgenogram of the chest showed elevation of the diaphragm, with the heart in transverse position and small areas of atelectasis in the lungs. A roentgenogram of the abdomen showed considerable density from free fluid. The spleen seemed enlarged, with the liver slightly smaller than usual.

The temperature spiked irregularly between 100 and 105°F for two weeks, then leveled off at 100°F. The patient grew progressively worse, and there was a slight increase in ascites. Abdominal paracentesis on the seventeenth hospital day gave 7000 cc of clear, yellow, sterile fluid, with a specific gravity of 1.018, there were 80 to 100 red cells per cubic millimeter and occasional white cells in

the sediment. Treatment included only transfusions, clyses and vitamins. After four weeks, there was bleeding from the mouth and the rectum; muscular wasting was most marked in the hands, forearms and legs. Terminally, the patient became stuporous, and the temperature rose to 106°F. Death occurred on the thirty-ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. THOMAS V. URMY: The story is that of a prolonged mild jaundice, a rather unusual recurrent skin eruption of many months' duration and a terminal phase beginning with an acute infection of the throat and characterized by rapidly developing hepatic insufficiency.

First of all, I must say that I can think of no one diagnosis that will explain the entire picture. So far as the chronic jaundice is concerned, we can eliminate hemolytic icterus because dark urine and light stools were present from the beginning, and also because later, when the patient was studied, the red-cell fragility and the urobilinogen were normal. Furthermore, many other tests indicated a biliary-tract lesion. I think that we can assume that this patient had primary intrahepatic disease, for it does not seem likely that the low-grade jaundice that he had originally could have been due to any form of obstruction. In further differentiation, catarrhal jaundice should be considered, but apparently he had none of the fever, nausea and vomiting that usually precede the onset of jaundice. It is, of course, unusual in such a case to have continued jaundice for over a year, although occasionally this occurs. I think we can dismiss catarrhal jaundice. Since the patient was a young boy developing chronic jaundice insidiously, we should consider Hanot's cirrhosis; however, we have no account of a large liver. It is stated that when he came into the hospital the liver was not definitely felt or enlarged by x-ray. However, the words of the case record, "the liver seemed of normal size," arouse some suspicion that the physical examination may not have agreed with later findings. Furthermore, to make a diagnosis of Hanot's cirrhosis, the liver need not have been enlarged when the patient came into the hospital because he had been failing fairly rapidly for two weeks before, and the liver might well have atrophied during that time. I should also mention that a toxic jaundice from some unknown cause might have started insidiously without prodromal symptoms and might have gone on to this terminal picture, but such a diagnosis is somewhat less attractive to me than Hanot's cirrhosis.

So far as the skin lesions are concerned, I can only make a guess. The fact that they were vesicu-

lar and bullous makes me think of pemphigus and dermatitis herpetiformis.

DR. TRACY B. MALLORY: The diagnosis of the dermatologist was dermatitis herpetiformis.

DR. URMY: That was also my diagnosis, mainly because the eruption was recurrent and itched badly, which I think pemphigus usually does not do. There were no mouth lesions or lesions on the hands, as one would expect in erythema multiforme. The interesting feature of this part of the history is that the patient was given arsenic. I wonder if the arsenic could have had a toxic effect on the liver.

Several other findings mentioned in the history should be considered, although they do not change my diagnosis. Attention is called to the fact that the posterior auricular lymph nodes were palpable, as well as nodes in the groins and axillas. The clinicians were apparently impressed by them, for they did a heterophil reaction to rule out infectious mononucleosis. Certainly, the appearance of the throat and at least the differential count, if not the total white-cell count, suggest it somewhat. Also, the presence of enlarged lymph nodes and an enlarged spleen raises the question of lymphoblastoma, but I cannot explain the whole picture on that basis. I shall regard the enlarged lymph nodes as incidental.

Finally, attention is called to the wasting that took place in the terminal stages of the disease, especially of the hands, forearms and legs. I wonder if we are being told of some type of peripheral neuritis or other local disease of the arms and legs in some way connected with the general picture. I think that we cannot assume peripheral neuritis without a history of pain. It seems wisest not to read any special meaning into this description. The patient may have had a very large abdomen, so that his general emaciation was more striking in the extremities.

When he was admitted, he was running a fever. He had a sore throat and had developed ascites. The liver may have been shrunken. What evidence we have indicates that. There was a moderate anemia, a low white-cell count, as we frequently see in intrahepatic disease, and many other indications of a diseased liver, such as a prolonged prothrombin time, an elevated van den Bergh reaction, a reversal of the albumin-globulin ratio, with marked reduction of the serum albumin, and a positive formol-gel test. Finally, the abdomen was tapped, and a fluid somewhat high in specific gravity but perfectly consistent with a transudate obtained.

It is impossible to make any more definite diagnosis than chronic liver disease. I shall call it Hanot's cirrhosis perhaps only because I have

never made the diagnosis before, and I should like to. I believe that there developed terminally an acute or subacute yellow atrophy secondary to acute tonsillitis and perhaps to the arsenic therapy.

DR. WYMAN RICHARDSON: I think this might be mycosis fungoides. Since one could say that all these symptoms might be associated with it, particularly in connection with the lymph nodes, I believe that one should consider more strongly the lymphocytic type of lymphoma as a possible explanation for the whole picture.

DR. URMY: I do not know much about it, but my impression is that this sort of skin picture does not occur in mycosis fungoides and is not so amenable to this type of treatment.

DR. RICHARDSON: Sodium cacodylate was formerly given for mycosis fungoides, with temporary improvement at least.

DR. MALLORY: That would be extremely unusual at this age.

DR. RICHARDSON: That is right. That would probably rule it out.

CLINICAL DIAGNOSIS

Hepatitis, nature undetermined, with terminal liver failure.

DR. URMY'S DIAGNOSES

Hanot's cirrhosis.

Acute yellow atrophy of liver.

Dermatitis herpetiformis.

ANATOMICAL DIAGNOSES

Cirrhosis of liver, healed atrophy (toxic) type.

Splenomegaly.

Ascites.

Icterus.

Pulmonary congestion and collapse, right lower lobe.

PATHOLOGICAL DISCUSSION

DR. MALLORY: I thought in reading this history over that the dermatologist had been courageous to treat a skin rash in a jaundiced patient with arsenic, and yet on each occasion the skin rash promptly disappeared, and the jaundice did not increase. The general condition was improved rather than otherwise so that I think the dermatologist was probably justified.

Autopsy showed a liver of normal, or slightly increased, size—weighing 1700 gm., very coarsely nodular, with big masses of young liver cells and large intervening areas of scar tissue containing innumerable bile ducts, the picture that we generally consider typical of the healed stage of acute atrophy. The microscopic examination added essentially no further information. There was no evidence of fresh or recent hepatitis. The acute

episode must have been some time long past. The spleen was very much enlarged, weighing 700 gm. Certainly, it should have been easily palpable. It showed rather marked fibrosis of the type seen in long-standing portal hypertension, whatever the etiology. The kidneys were large, weighing 500 gm., were moderately bile stained, and showed pouting of the substance over the capsule, and the moderate degree of tubular degeneration that is called "bile nephrosis." I assume that it was merely secondary to the long-standing secretion of bile salts in the urine. There was nothing else.

DR. RICHARDSON: Were there any lymph nodes around the abdomen or thoracic cage?

DR. MALLORY: None that were noticed as being unusual in size.

DR. URMY: Would you guess how long it was since the atrophy had occurred?

DR. MALLORY: A year at least—perhaps much longer.

DR. URMY: Why did the patient die at this time?

DR. MALLORY: I think he unquestionably died of liver insufficiency, in spite of the size of the liver. It was a liver incapable of normal function. I am afraid that it is beyond the realms of morphologic pathology to explain why.

DR. URMY: Did the lesions suggest that the patient had improved?

DR. MALLORY: There was no active progressive hepatic-cell degeneration, but immense amounts of scar tissue had formed, some of which may have caused intrahepatic obstruction of the bile ducts or portal radicles, and the extensive reconstruction may have made the vascular architecture of the liver inadequate.

A PHYSICIAN: Do you recognize any pathologic picture that goes with dermatitis herpetiformis? What is the usual outlook in this condition?

DR. MALLORY: I am afraid I cannot answer that.

A PHYSICIAN: The condition is very difficult to treat. It is a chronic disease that usually ends fatally with some terminal infection, just like pemphigus. It is difficult to separate the two.

DR. MALLORY: I do not know of any typical post-mortem picture.

CASE 28282

PRESENTATION OF CASE

A fifty-five-year-old bartender was admitted to the hospital because of recurrent spitting of blood.

The patient was in excellent health until a year before entry, when he had a ten-day illness characterized by malaise, anorexia, coryza, dry cough, shaking chills and, probably, fever; he had no chest pain or sputum. Recovery was complete except for persistence of the dry cough. Six months before

entry, the intensity of this cough increased, during the course of a coryza, and the patient began to spit up small lumps of blood mixed with a little mucus. This continued. At first, this sputum was foul tasting, but after a week it was no longer so. Not over one or two tablespoonfuls of sputum was brought up in the course of a day, and sometimes no blood was seen for several days. In the first two weeks of this phase of the illness, there was anorexia, and a loss of 5 or 6 pounds in weight, which was subsequently regained. There were no pains, chills or fever at this time. Two months before entry, the patient consulted his physician. He was told that a roentgenogram showed "a little growth in a bronchus" and was referred to the hospital.

The patient's son had died of meningeal and renal tuberculosis. The family and past histories were otherwise of no interest. No recent dental work had been done.

On admission, the patient appeared slightly obese. The heart was slightly enlarged toward the left. The lungs were normal. The liver edge lay two fingerbreadths below the costal margin. The abdomen was otherwise normal. Bilateral indirect inguinal hernias were present. Rectal examination was negative. The fingers were not clubbed, and the legs were not tender.

The blood pressure was 130 systolic, 90 diastolic. The temperature was 99°F., the pulse 80, and the respirations 20.

Examination of the blood showed a red-cell count of 5,110,000 with 14 gm. hemoglobin, and a white-cell count of 7900 with 76 per cent polymorphonuclears, 14 per cent lymphocytes and 9 per cent monocytes. The blood Hinton reaction was negative. The urine was normal. The sputum showed no acid-fast bacilli in three examinations, but grew alpha-hemolytic streptococci in three cultures. A tuberculin test in a dilution of 1:20,000 was positive.

Roentgenograms of the chest showed a round area of consolidation, 5 cm. in diameter, in the apex of the left lower lobe, which contained a cavity without a fluid level. The left hilum was slightly lower than usual, and included a small area of calcification. The diaphragm showed normal motion. In comparison with the film taken two months before entry, the process in the apex of the left lower lobe seemed slightly decreased in size.

The temperature fluctuated from 98.6 to 100.0°F. daily. On the fifth hospital day, bronchoscopy was performed. The larynx, trachea, right bronchial tree, left main bronchus and left-upper-lobe orifice appeared normal. There was considerable blood in the trachea and left main bronchus, which

apparently came from the dorsal branch of the left lower bronchus. The distal margin of this orifice appeared slightly roughened and irregular. A biopsy obtained from this area showed chronic inflammation. The terminal branches of the left main bronchus appeared normal.

The patient was given a three-day course of sulfathiazole and attained a blood level of 5.5 mg. per 100 cc. Because of nausea, sulfadiazine was substituted, and a blood level of 11 mg. per 100 cc. was reached. He continued to raise a little blood-streaked sputum. On the seventh day of sulfadiazine medication, there was a sudden rise in temperature to 105°F., accompanied by a chill and by the appearance of a faint macular rash. The chest remained clear. Drug therapy was discontinued, and the temperature returned to its previous level in a few days. A roentgenogram taken three days before this reaction showed sharper delimitation of the shadow in the left lower lobe, with a definite fluid-free cavity included in it.

On the thirty-second hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. DONALD S. KING: To summarize briefly, the patient gave a history of infection of a year's duration, with chills, with a dry cough for six months and without fever. He then began to raise blood and continued to cough up blood and blood-streaked sputum for another six months, and had a little fever toward the end. He appears to have had some expectoration other than blood, and it is reported that it tasted badly; however, since we did not have the opportunity to smell the sputum, we cannot be sure that it was foul. We can assume that a note would have been made if it had been notably foul when the patient was in the hospital. The physical examination was remarkable because it did not show much of anything. The general condition was good,—somewhat against cancer,—and the lungs were normal; that is certainly not what we should expect in this case. There were no signs of consolidation, no diminished breath sounds, no moist rales and no musical rales. Outside the lungs, there were no palpable lymph nodes, no clubbed fingers and no source of emboli. We are left practically stranded on physical findings.

The laboratory findings help not at all except for three cultures that showed alpha-hemolytic streptococci. That may be of significance, although I should have been much more influenced by the demonstration of streptococci in smears of the sputum than in these cultures.

I shall now take up the x-ray films. I am not

so impressed with the "round tumor" as I had expected to be from reading the record.

DR AUBREY O. HAMPTON: In this film, the lesion looks like a fairly round mass. I agree that the shadows in the other films do not look at all spherical. The cavity is not very plain. It is very small and irregular. The wall of the cavity is quite thick and irregular on the inside. This triangle is the only suggestion of bronchial occlusion. I believe it indicates pleural involvement. Otherwise, there is nothing in the lung to suggest a bronchial occlusion. The bones are normal.

DR KING: This is the film at expiration, corresponding to this one at inspiration?

DR HAMPTON: Yes; it does not show any air trapping or mediastinal shift.

DR KING: Did the mass really decrease in size?

DR HAMPTON: There was a reduction of 2 cm in the diameter in the two month interval.

DR KING: This x-ray picture is not typical of anything.

Three things should be borne in mind, — cancer, tuberculosis and abscess, — and perhaps some other conditions, but these primarily. This case is not typical of cancer in my opinion. There was not the density of tumor or the sharply defined margin that one might expect. It is hard for me to accept the diagnosis of cancer. Furthermore, there is no evidence of bronchial obstruction that I can see anywhere except possibly the area that Dr Hampton pointed out, which could be infiltration and not atelectasis. I am therefore inclined to throw out cancer but should not be at all surprised if the patient had it. I cannot, however, make the diagnosis. The x-ray film does not look like it. The story is possible for it.

This case is also not typical of tuberculosis. There was not the mottling of ordinary tuberculosis, and there was no suggestion of a tuberculoma that was breaking down in the center. The most certain thing about tuberculosis is its uncertainty, and this may have been some form of tuberculosis after all. One point against tuberculosis is that, with a six months' story of hemoptysis and x-ray observation for two months, the patient should have had a more typical cavity in the lung. It is my belief that it was not tuberculosis. The negative sputum does not rule out tuberculosis, in spite of the fact that the patient was raising sputum and should have shown organisms.

One has to think about abscess, of course, because of the mention of the foul taste of the sputum. There was no putrid abscess. To make it abscess, one must make it a putrid, on a streptococcal basis. We have one case that came to au-

topsy with a lesion much like this from which the pyocyanus bacillus was recovered in pure culture. If one pays a great deal of attention to sputum cultures, streptococcus is a perfectly good bet. The nearest case in our series to this, as I see it, is one of a patient who was operated on for tumor, and the lesion proved to be a streptococcal abscess. The patient in the case under discussion also started with bloody sputum and was still coughing blood at the end of three months. I think a streptococcal process might carry on this way longer than tuberculosis, so that of the three main possibilities at the moment, I should vote for streptococcal abscess.

Another vague possibility is bronchiectasis. Dr. Hampton at one time claimed to be able to see dilated bronchi on the plain film.

DR HAMPTON: I do not see any.

DR KING: The location is unusual for bronchiectasis, and if one counts this as cavity in the middle of the lobe, one must assume involvement of the parenchymatous tissue as well as bronchiectasis. There might have been some bronchiectasis associated with the process, but it was not primary bronchiectasis. Other unusual infections suggested are blastomycosis and actinomycosis. There were no skin lesions and no chest-wall sinuses to go with such diagnoses, hence, there is no reason to think of them. Then, we have our old friend, lymphoma, which we shall think about and pass over. From the x-ray standpoint, we have seen the same picture, but the story is not like it, and I am willing to throw it out. Therefore, I should say that the chances are that this was a streptococcal abscess. I shall, with some disquietude, throw out cancer and tuberculosis.

The operation interests me. I assume that a lobectomy and not a drainage was performed.

DR PAUL D. WHITE: I was visiting on the service when this man was being studied. The interesting point at that time was that in the beginning everyone, including the members of the Thoracic Clinic, guessed that the patient had a tumor of the lung. For example, Dr. Victor Balboni, on admitting the patient, believed that this was a bronchial tumor, probably adenoma, both by story and by x-ray.

DR KING: I should like to mention adenoma. I meant to put it in the differential diagnosis. The persistent bleeding is consistent. There was no bronchial obstruction, however. If an adenoma had caused this bleeding there ought to have been atelectasis, and I therefore discard adenoma.

DR WHITE: The first statement from the Thoracic Clinic was as follows: "We favor cancer as being more probable than a benign tumor. The

chances are that the growth may be beyond the reach of the bronchoscope. In either event, with or without positive biopsy, benign or malignant, exploration should be considered." As x-ray evidence developed, there was a shift of diagnosis by the members of the clinic to infection rather than tumor, and that, I think, was the status at the time of exploration. The fever, however, which was one of the features that developed, might, we thought, be explained by drug reaction.

DR. LOWREY F. DAVENPORT: We went all around the clock in the Thoracic Clinic, and when the case came to operation, the consensus was infection or tumor and, if tumor, either benign or malignant. At any rate, we took out the lobe.

DR. HAMPTON: Did you not rule out tumor on the basis of the reduction in size of the mass?

DR. DAVENPORT: As I said, we went around the clock, first favoring malignant tumor and then, following subsequent x-ray studies, abscess. We eventually decided to operate.

DR. JACOB LERMAN: It seems to me that as the mass reduced in size it became sharper. Could it not have been tumor, with secondary infection and obstruction?

CLINICAL DIAGNOSIS

Carcinoma of lung?

DR. KING'S DIAGNOSIS

Streptococcal abscess of lung.

ANATOMICAL DIAGNOSIS

Epidermoid carcinoma, bronchiogenic, left lower lobe.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: As Dr. King predicted, a lobectomy was decided on in this case, whatever the diagnosis might turn out to be. That was carried out by Dr. E. D. Churchill, and in the resected specimen we found a well-circumscribed epidermoid carcinoma, with a central cavity, 1.5 cm. in diameter, evidently the result of breakdown of the tumor tissue. All the walls of the cavity consisted of carcinoma. The tumor was exceptionally well differentiated. It lay fairly well out in the lung parenchyma, without demonstrable invasion of the hilar nodes, and this looks like one of the most favorable cases in the series for cure.

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ANNUAL MEETING OF THE AMERICAN MEDICAL ASSOCIATION

THE annual meeting of the American Medical Association was held at Atlantic City from Monday, June 8, through Friday, June 12. The gasoline and rubber shortage or fear of the dimout or that Hitler might take the opportunity to get rid of a few thousand physicians did not lessen the attendance or enthusiasm at the meeting. To be sure the boardwalk was not its gay and dazzling self at night, but it was colorful enough in the daytime.

Mr. Paul V. McNutt, administrator of the Federal Security Agency, was the principal speaker at the dinner given in honor of the officers and delegates on Monday evening. His remarks, some-

what misquoted in the daily papers, were forceful and pointed. He said that the Procurement and Assignment Service had been set up largely at the suggestion of members of the medical, dental and veterinarian professions and that these doctors constitute the only group that has been allowed to manage its own affairs in the emergency. He added that he hoped the Procurement and Assignment Service would succeed and that he and his associates would do all they could to keep it working. He admitted, nevertheless, that, up to the moment, not enough physicians had been obtained for the armed services and that if they were not forthcoming in the near future, some means other than the Procurement and Assignment Service must be utilized. His emphasis left no doubt as to his meaning. He addressed the House of Delegates in similar vein at its business meeting the next morning.

The meetings of the House of Delegates were, as usual, well attended and businesslike. There was some agitation to increase the size of the Board of Trustees from five to nine, on the theory that a considerable portion of the country was not represented. It was pointed out, however, that the Board of Trustees was not intended to be a representative body but was designed to conduct the business of the association and that small business boards are usually more efficient than large ones. The House of Delegates declined to authorize the change.

The resolution of the Massachusetts Medical Society regarding prepayment sickness insurance was presented, and the delegates voted to approve the provision of prepayment medical insurance on a medical-service as well as a cash-indemnity basis. The House of Delegates also authorized the Council on Medical Education and Hospitals to set up a program for refresher courses for physicians returning to private practice after the war, to bring them up to date in medical progress. This was accompanied by instructions to the Board of Trustees to urge military authorities to continue to pay full allowance to physicians who desired to take these courses.

The huge auditorium provided adequate space, not only for the scientific and commercial exhibits but also for the section meetings, the former continuing to grow in size and interest each year. All in all, the meeting was well up to its usual standards.

DEATH RATE IN INFANCY AND CHILDHOOD

DURING the past two decades, according to Dublin and Spiegelman,* child mortality in the United States has maintained not only a consistent but a spectacular fall. In 1920, for example, an infant mortality rate of 86 per 1000 live births obtained in the birth registration states of 1917; in 1929, this had declined to 66, and in 1939, to 44. That even greater improvement under continuing conditions of peace and relative freedom from epidemic disease might be expected is shown by the inequality of the general rate, ranging from a recent high of 109 deaths per 1000 births in New Mexico to a low of 37 in Connecticut, New Jersey, Oregon and Washington.

Although, on the whole, infant mortality is lowest in the north central and northwestern states, and highest in the South, it is interesting that Maine, of the New England states, stands alone in its membership among the states with the highest rates—over 50. New Hampshire and Vermont rank in the next group, with a 45 to 49 rate range, and Massachusetts and Rhode Island in the group with rates from 40 to 44. Connecticut is the only state in the most favorable group, with a rate below 40.

It is eloquent of the effects of civilization and economic advance, however, that during this period, for the first time in the history of the United States, an actual decrease in the child population has occurred. Such has been the decline in the birth rate that the number of children under fifteen years of age, which had risen from 33,600,000

in 1920 to 36,100,000 in 1930, diminished to 33,100,000 in 1940, or from 32 per cent of the total population in 1920 to 25 per cent in 1940. At the same rate, the number will have decreased to about 32,000,000 in 1960, or 22 per cent of the total population.

The improvement in child mortality, if not in total child population, is no doubt an index of the general rise in the standards of living, including improved benefits from medical science and public-health administration. It may be that the flood tide in the benefits that science can give to mankind has been reached: standards of living are going to be lowered; materials will be directed into other channels of production; scientific effort will be directed away from the paths of peaceful advance; personnel will be engaged elsewhere.

Greater effort than ever before will be required of those who can still participate in peaceful projects to hold fast to the ground that has already been gained.

MEDICAL EPONYM

POLITZER BAG

Dr. Adam Politzer (1835–1920), while *Docent* in otology at the University of Vienna, presented a discussion, "Über ein neues Heilverfahren gegen Schwerhörigkeit in Folge von Unwegsamkeit der Eustachischen Ohrtrumpete [On a New Therapeutic Procedure in Deafness due to Blocking of the Eustachian Tube]," in the *Wiener medizinische Wochenschrift* (13:84-87, 102-104, 117-119 and 148-152, 1863). A portion of the translation follows:

The seated patient holds a little water in his mouth . . . and is told beforehand to swallow it at a given signal. The instrument used consists of a straight or slightly curved metal tube shaped like a catheter; or better, a rubber tube of rather large caliber, connected with a pear-shaped rubber bag about twice as big as a man's fist. The physician, standing preferably at the patient's right side, inserts the anterior end of the tube 1.0 cm. into the proper nostril, compresses the ala nasi (so that no air can pass over the instrument) with his left thumb and index finger, and with his right hand vigorously expresses air from the bag into the nose while the patient swallows.

R. W. B.

*Dublin, L. I., and Spiegelman, M. The control of disease and death in infancy and childhood. *The Record* (American Institute of Actuaries) 30:28-57, 1941.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY: PREMATURE SEPARATION
OF THE PLACENTA, FOLLOWED BY DEATH

A multipara was not seen until she arrived in the hospital when about six months pregnant. Her past history was essentially negative, and she had had no prenatal care. Her first four pregnancies had been normal, and all the children were living. She entered the hospital because of bleeding, which had started as a stain when in the tenth week of pregnancy and had continued off and on as a stain until shortly before hospital entry. Three weeks before admission, she had had a sudden profuse flow with clots, and had stayed in bed at home until she went into the hospital. On entry, she was flowing moderately and continued to flow sufficiently to require six or eight pads a day for the next two weeks and a half. No examination was made during this time, presumably because the pregnancy had not advanced to a point where a viable child was likely to be obtained and for fear of increasing the bleeding by examination. At the end of this time, the bleeding increased, and vaginal examination was done. This revealed no placenta previa, and by the process of elimination, a diagnosis of separated placenta was made. The following day, the membranes were artificially ruptured, the cervix and vagina were packed with gauze, and a Spanish windlass was applied. The next day, the baby and placenta were delivered. Since the placenta did not come away spontaneously, manual extraction was performed and was followed by very free bleeding. An hour and a half after the placenta had been extracted, 500 cc. of blood was administered. Since the bleeding increased, the vagina and uterus were packed with gauze, and a second transfusion was given. Finally, because of continued bleeding, an abdominal hysterectomy was performed, but the patient did not survive the operation. Autopsy showed a post-partum uterus with portions of adherent placenta.

Comment. The history of this case is rather unusual. Throughout the period of irregular flowing, medical advice was not sought until a frank hemorrhage had occurred. Delayed treatment in the hospital for the presumable purpose of securing a viable child was warranted. Furthermore, rupture of the membranes and packing of the cervix and vagina were undoubtedly the method of choice in a multipara at this stage of pregnancy when another hemorrhage demanded surgical intervention. Had the placenta been examined very carefully, it might have been inferred

that the hemorrhage following delivery was due to pieces of placenta that remained after manual extraction. Although the record makes no mention of it, it is also possible that this adherent placenta was a true accreta, and had this been recognized, if such existed, at the time of manual removal, an immediate hysterectomy following the first transfusion might have prevented the fatality.

If this patient had been seen earlier in her pregnancy at the onset of bleeding, it might have been deemed wise to curette the uterus then. If this had been done, the fatality would never have occurred.

DEATHS

METIVIER — **ARMAND O. METIVIER, M.D.**, of Chicopee Falls, died July 2. He was in his fifty-third year.

Born in Canada, he later went to Keene, New Hampshire. He graduated from St. Anselm's College and received his degree from the College of Physicians and Surgeons, Boston, in 1915.

Dr. Melvier was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son, two daughters and four brothers survive him.

WILLOUGHBY — **EARLE C. WILLOUGHBY, M.D.**, of North Reading, died June 23. He was in his sixty-first year.

Born in North Haverhill, New Hampshire, he received his degree from Tufts College Medical School in 1911. He served on the staff of the State Infirmary at Tewksbury until 1917, when he was transferred to the North Reading State Sanatorium. Soon after that, he was made assistant superintendent.

Dr. Willoughby was a fellow of the Massachusetts Medical Society and the American Medical Association. He was also a member of the Southern Middlesex Health Association, the Trudeau Society of America and the National Tuberculosis Association.

His widow and two brothers survive him.

MASSACHUSETTS MEDICAL SERVICE

WIDE INTEREST IN PLAN

All licensed physicians in Massachusetts may participate in the Massachusetts Medical Service, according to Dr. James C. McCann, the newly elected president. Since the public announcement of the launching of the new nonprofit system for the prepaid budgeting of medical care, the headquarters at 230 Congress Street, Boston, have been flooded with inquiries from physicians and laymen throughout the state.

"The chief query from the public," McCann states, "is, When will the service be available? The speed with which doctors participate is the only answer, although early September is our goal. While the first contract is limited to surgery, obstetrics and diagnostic x-ray service, all physicians are urged to pledge their support, even

if they are not involved in the first contract."

Because physicians are asking for more detailed information about the new nonprofit corporation, a series of articles has been prepared by the members of the Central Professional Committee. The first of these, dealing with the corporate structure of the organization, appears below. In the following weeks, the *Journal* will publish articles dealing with service contracts, compensation for professional service, the physician's relation to the corporation, the relation of the Massachusetts Medical Service to hospitals and the enrollment regulations of the plan.

* * *

THE CORPORATE STRUCTURE

JAMES C. MCCANN, M.D.

Voluntarily, the medical profession is altering its economic relations with the public through the establishment of the Massachusetts Medical Service, which is set up as a nonprofit corporation. Complete legal protection for the new endeavor is provided by the corporate structure.

Since physicians are placing control of many aspects of medical practice in the hands of a corporation, they may rightfully ask, How does the corporation function? It will function as does any business corporation. Members of the Executive Committee of the Massachusetts Medical Society constitute the voting members of the corporation and take the place of stockholders. The voting members elect the directors, who, in turn, are the corporation's managers. The voting members can remove the directors from office if there is due cause. The only other restrictions on the directors' powers are those specified in the by-laws, those arising from the state insurance commissioner's interpretation of the enabling act and the by-laws and those arising out of recourse by any party to the courts.

Security of Physicians

It is vital that medical standards relating to the welfare and the rights of physicians be protected when they become involved with the legal complexities of a corporation, and that there be professional supervision of the purely medical aspects of any such plan. This supervision is guaranteed by the fact that the voting members are, themselves, physicians representing the profession of the entire state.

As described in the June 18 and July 2 issues of the *Journal*, the directorate of the Massachusetts Medical Service numbers fifteen members, representing equally physicians who have direct contact with the medical profession through the local professional service committees in the districts, eminent laymen whose practical experience is of great value and outstanding representatives of the subscriber groups.

Vital medical matters might be mishandled by such a composite corporation were it not for the organization and the functioning of the Board of Directors, which is broken into committees assigned to specific tasks. The Executive Committee takes responsibility between the meetings of the entire directorate. The Financial Committee guards the funds and investments. The Actuarial Research Committee compiles data that protect physicians through a sound actuarial procedure. The Interlocking Services

Committee supervises the relation of the two independent but jointly functioning corporations — Massachusetts Medical Service and the Blue Cross. The Central Professional Committee has power to initiate action for the Board of Directors on all vital medical matters, submitting complete medical data as a basis for any action by the board. In effect, the last committee serves as a medical advisory committee to the directorate. Furthermore, any anticipated action by the Central Professional Committee must be reported to the voting members, thirty days before action is taken, and the latter can send resolutions and recommendations to the directors. This assures to the representatives of the profession full knowledge of anticipated action by the directors on medical matters. Such facts will also be available to the Council of the Massachusetts Medical Society, whose resolutions or recommendations to the voting members would carry impressive weight.

The medical profession of Massachusetts is privileged to have serving on the directorate some of the most eminent nonmedical leaders of the state. These men are serving without compensation, because of a sense of responsibility to the public, and have accepted a trusteeship that will require much of their time and expert judgment. Remembering that the corporation is not an insurance company but strictly a corporation formed by them to solve current problems in medical care, physicians are greatly indebted to these civic-minded lay directors.

Opportunity for Plan

Massachusetts Medical Service, established after long years of study and based on the experience of other medical-care plans throughout the country, has the opportunity of meeting changing conditions and, at the same time, of preserving basic freedoms. Patients retain the freedom of choice, and physicians retain the freedom to serve. Through this new corporation, the medical profession of Massachusetts can satisfactorily meet the challenge of the times.

WAR ACTIVITIES

CIVILIAN DEFENSE

AIDS TO DECONTAMINATION

The following letter has recently been received by the Office of Civilian Defense, Washington, D. C.:

Decontamination stations should be of simple construction with ample facilities for disrobing, bathing and chemical neutralization. Persons contaminated with liquid vesicants must be treated within five minutes to avoid severe burns. Complete preparations therefore require that facilities are sufficiently numerous so that every individual is within five-minutes walk of a decontamination station. Gasoline filling stations are widely distributed and may be adapted for this purpose.

Suggestions for adapting gasoline filling stations for decontamination are as follows:

1. Use stations with washing and greasing facilities under cover.
2. Establish a temporary disrobing area outside and adjoining the washroom, shielded by canvas, parked automobiles or some other device providing privacy. Allow abundant natural ventilation. Everyone entering the disrobing area must walk through a box of sand and bleaching powder to decontaminate his shoes (three parts of sand to one part of bleach containing 30 per cent hypochlorite).

3 Provide a gas lock to the washroom, with a foot bath of bleach slurry of sodium hypochlorite solution

4 Install temporary showers or improvise a pipe with several outlets for multiple bathing. Use hoses operated by attendants for washing large numbers of people. Supply soap

5 Eyes should be irrigated with soda near the entrance of the washroom or hosed gently with plain water in the event of large numbers

6 Use grease room for dressing

7 Partition off the grease room from the wash room with wall board or other temporary material if the rooms are not already separated

8 Provide a gas lock between the washroom and the dressing room

9 Use the station office or the ladies rest room for first aid, if necessary

10 It is advisable to ventilate the wash and dressing rooms by means of ordinary cooling fans blowing out of the windows

11 Supply numbered paper, burlap or cloth bags for each person's clothing, and record name and address opposite the number

12 Keep contaminated clothing outside the station, and place bags of clothing in covered metal containers until decontaminated

13 Provide a supply of clean clothing of assorted sizes in the dressing room

14 Apply bleach or sodium hypochlorite solution such as Chlorox, Zonite and so forth as indicated for liquid contamination either in the disrobing room or washroom.

15 It is advisable to paint wall board, wood, concrete or brick with sodium silicate paint to prevent persistent contamination

16 Consult the Office of Civilian Defense publications *Protection Against Gas*, and *First Aid in the Prevention and Treatment of Chemical Casualties* for detailed instructions

The organization and direction of decontamination services for persons is under the Emergency Medical Service. Decontamination of uninjured persons may be assigned by the chief of Emergency Medical Service to the local health department. Stations for decontamination of persons may be operated under the supervision of public health nurses where physicians are not available. Decontamination of food and water supplies should be assigned to the local health department.

CORRESPONDENCE

TREATMENT OF PATIENTS SUFFERING FROM DIETARY DEFICIENCIES AND PROLONGED EXPOSURE

To the Editor I have just seen a perfectly extraordinary situation about which I think something should be done although I am completely at a loss how to proceed

A thirty-two-year-old sailor just came to my office because of excruciating pain in his legs, for which he wished some morphine. One month ago he was on a boat torpedoed off Cape Hatteras. For thirteen days he was in an open boat, with nothing to eat except hardtack and water. Nine of his companions died before the others were picked up a hundred miles offshore by a coastguard boat. All the ten who were saved had enormously swollen feet and legs, and most of them said they felt dead below the knees. Their bodies were covered with salt water boils, and the skin of their hands and feet was soft and white from constantly being soaked in salt water.

The rescued men were taken to a hospital in Delaware. They were put on a light diet, consisting of milk, as often as they wished one egg a day and one small portion of meat a day, they had all the fruit they wished. The first two or three days they had contrast baths, and then they were started on suction treatment with a glass boot, forty minutes a day, for their swollen feet. They received no Brewer's yeast, liver extract or other vitamin preparations either parenterally or by mouth. Some including my patient, received sulfanilamide because of furunculosis.

After two weeks of this treatment, my patient decided to leave the hospital as he was not getting any better. The physicians there told him there was nothing that could be done for his painful legs except the boot treatment and eating a lot. They also said that no other treatment was being used anywhere along the Atlantic seaboard, where so many similar cases are being treated in the hospitals along the shore.

My patient is still some 18 to 20 pounds below his weight of a month ago and has absent vibration sense below his ankles that is, over both feet. He has no paresthesia above the ankles but complains bitterly of a dull aching pain in the bones of his feet.

I do not believe there is the slightest doubt that he will eventually have practically complete clearing of all his paresthesia on nothing but an average diet. It seems pretty inexcusable to me, however, to treat men suffering from acute vitamin deficiency with contrast baths and a suction boot without any vitamin supplement orally or parenterally.

My particular patient being relatively young is probably going to get by without any permanent damage from the treatment he received, but I wonder if something should not be done to wake up the medical men responsible for the care given in these hospitals.

DUDLEY MERRILL, MD

51 Brattle Street
Cambridge, Massachusetts

REPORT OF MEETING

HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on March 10 with Dr. James P. O'Hare presiding.

In a case presented by the Surgical Service, a seventeen-year-old boy entered the hospital half an hour after receiving second-degree and third-degree burns of more than half the body surface in a gasoline explosion. The area was immediately cleaned and debrided in the operating room under Penitrothal anesthesia. An eschar of trinitro acid and silver nitrate was applied to the flat surfaces and tulle gras to the areas where motion was advisable. During the first ten hours the patient was given enough fluid

min and plasma in 12,000 cc. of fluid to equal 8000 cc. of plasma, yet the hemoglobin concentration remained at double its usual value. After twenty-four hours, the face, neck and tongue began to swell dangerously, and multiple Z incisions were made in the neck to relieve the severe constriction. The patient gradually improved and received decreasing amounts of parenteral fluids until the sixth day, when he was able to maintain himself by oral feedings. The burns remained nonseptic, and after several weeks, epithelialization began in several areas.

In discussing the case, Dr. Charles A. Janeway stated that the 100 gm. of albumin, which equals 2000 cc. of plasma, was just sufficient to maintain daily equilibrium at first. The parenteral use of crystalloids not only is disadvantageous but may actually be harmful in that it may increase hemoconcentration and further deplete the plasma protein. This patient, as a result of the albumin therapy, finally reached a state where the total protein value, although normal, consisted of practically all albumin and no globulin. The value of the latter component for many vital substances, notably vitamin K, makes it advisable to change to plasma therapy at an early stage in the treatment of prolonged protein loss. The elevated nonprotein-nitrogen level encountered in this case and other cases of severe burns may be attributable to increased tissue destruction or the hypothetical toxins elaborated in the burned areas. It should be noted, however, that plasma, especially the commercial product, contains appreciable amounts of Merthiolate, which is toxic because of its mercury content. The cost of such therapy is about \$35.00 for 1000 cc. of plasma.

Dr. Elliott C. Cutler, the speaker of the evening, reminded the group that it would require 16,000 cc. of blood merely for the first few days' treatment of this single patient, and therefore questioned the practicability of blood banks as a means of combating mass shock, unless such banks can be conducted on a grand scale. Tanning of burned areas is acceptable and probably preferable on flat surfaces, but is definitely contraindicated where there are creases, where the part is mobile or where an entire circumference is involved, when an eschar may cause interference with circulation or choking, as in the case presented.

Dr. Cutler discussed "The Medical Aspects of Civilian Defense." In emphasizing the need for immediate perfection of home defense, it was pointed out that the United Nations have so far guessed wrong on practically every major move on the part of the enemy, and that our only protection is an all-out preparation. We may even sustain gas attacks, which were abandoned in the assault on England only because of the fear of retaliation. Scrutiny of the trained personnel on hand and the estimated number needed makes it apparent that there is no inadequacy in this respect.

Dr. Cutler reviewed the map of Massachusetts, with its defense regions. Region 5, including Greater Boston with its two million inhabitants and the majority of defense plants, has about 50 per cent of the entire population. The regional organizations are capable of working independently of the central committee. The deputy regional medical officers represent the various medical societies, and these men must therefore be free to work at any time. Dentists are also needed for this purpose, for exact information may often be essential in either medicine or dentistry at the report centers. Hospital superintendents are also being placed in a similar role for organization of institutions.

Cities and towns have their own medical committees, which follow a general plan of organization and action so that the entire group may be integrated in the event of a widespread incident. There are first-aid posts, ideally composed of duplicate units, each with two physicians, two nurses, four nurses' aides and four men trained in first aid. Secondly, there are the first-aid parties comprising lay people, preferably trained in ARP schools and Red Cross courses. In general, it is strongly urged that all the members of all special groups, such as first-aid, wrecking and public-utilities parties, attend an ARP school before taking their postgraduate training in their specialty. Although transportation worries the general population, it is in reality relatively simple. Hospital administration, however, entails a problem. It is necessary to fulfill the requirements of the Governor's proclamation regarding blackouts while attempting to adhere to a strict budget. It is suggested that money not be wasted on unessential embellishments. Plans have been made for the use of certain institutions as base hospitals in the event of bombings in metropolitan areas, but no promise can be given that evacuation from a given place will be to a certain base hospital.

In addition to the central executive committee, there are subcommittees on base hospitals, on the medical aspects of evacuation, of medical examiners, of dentistry, of public health, of liaison with the Red Cross and with the Protection Division, and on pharmacy. The last group has donated all the necessary pharmaceuticals. Certain drug-stores have been designated as auxiliary first-aid supply depots, but they must pass certain requirements.

A brief sketch was given of the course of events if an incident occurs: the role of the interceptor command, which ranges three hundred miles to sea; the meaning and scope of the blue, yellow and red signals; and some of the intricacies and major duties of the many report centers scattered throughout each section. In many of the smaller towns, the medical supply depot, Red Cross depot and casualty station are located together in some central public building, which may also be the report center. The casualty station serves to relieve congestion in necessary hospitals by caring for minor wounded and ambulatory patients. When an incident occurs, mobile medical units (medical first-aid posts and lay first-aid parties) are dispatched to the site by ambulance. The former group sets up the post in some appropriate house or building nearby and determines, according to the extent of the incident, what cases may be treated there and what cases should be transferred to hospitals. These are first sent to emergency hospitals and are then transferred to base hospitals if evacuation of the former becomes necessary.

During the discussion it was emphasized that sulfanilamide powder may be full of spores and is not self-sterilizing. This fact also makes its sterilization in containers difficult, but this has finally been overcome, and the drug is now dispensed in individual sterile containers.

BOOK REVIEW

Roentgen Technique. By Clyde McNeill, M.D. Second edition. 8°, cloth, 329 pp., with 276 illustrations. Springfield, Illinois: Charles C Thomas, 1941. \$5.00.

This book is clear, concise, well diagramed and thorough, especially in its discussion of x-ray technic of the skull. It is a good handbook for roentgenologists and technicians.

(Notices on page viii)

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CEREBRAL SUBDURAL HEMATOMAS*

A Study of Three Hundred and Ten Verified Cases

DONALD MUNRO, MD†

BOSTON

IN 1933, I¹ read a paper before this society on the diagnosis and treatment of subdural hematomas. This was based on my experience with 62 cases. By 1938, the number of cases that I had studied had increased to 215.² By January, 1941, 95 more cases had brought the total to 310. It is this group that forms the subject of this paper. As my experience has increased, it has become more and more apparent that the accuracy of one's conclusions varies directly with the number of cases from which the conclusions have been drawn. This truism is justified by the persistence with which small numbers of cases are published and made to serve as bases for conclusions that are in disagreement with or ignore those drawn from larger and more adequate series.³⁻⁴ Notable among the exceptions to this statement are papers by Browder and his co-workers,⁵ Davidoff and Dyke,⁶ and Ingraham and Heyl.⁷ Examples of its truth are a recent editorial⁸ based on two articles in one of which the author's experience was limited to 48 patients, the other being a synthetic report of 42 cases of which the author himself had seen 2, and a case report⁹ presumably published to help care for injured naval personnel. The last is said to describe a case of "pachymeningitis hemorrhagica," but it presents all the autopsy findings of an intracortical clot. There is no doubt in my mind that personal experience with no less than 100 cases of significant subdural hematomas is indispensable to a competent opinion about the incidence, classification, pathology, diagnosis, treatment and prognosis of this very common condition.

In all the 310 cases reported herewith, the presence of the clot was verified either at operation or at autopsy, and was the only significant, or in mul-

tiples lesions, the most significant, intracranial lesion present. Although the clots were not weighed and the amount of subdural fluid was only roughly estimated, the size of the former and the amount of the latter were always pathologically significant. No case has been included in which the clot or the fluid could, by any stretch of the imagination, be considered incidental either to other findings or in their own right.

The gross pathology of subdural hematomas has been described by Leary and Edwards,¹⁰ Leary¹¹ and Peet and Kahn.¹² Their work, especially that done by Leary, supersedes, amplifies and corrects the findings published by Putnam and Cushing.¹³ Gardner¹⁴ has covered the experimental field, those unfamiliar with his work should consult the original article. It is fundamental and unquestionably accurate. The surgical pathology has been covered by Munro and Merritt¹⁵, increasing experience has confirmed these earlier findings. So far as I know, no comparable studies have been published since then. I have no doubt, therefore, from these data and other evidence, as well as from my own increasing experience, that cerebral and cerebellar subdural hematomas originate as blood and cerebrospinal fluid mixed in varying amounts and incarcerated within the intracranial subdural space.

In conformity with what appears to be a fixed determination on the part of the medical profession to divide subdural hematomas into acute and chronic groups, the cases in this series have been grouped accordingly. However, since attempts to measure the acuteness by elapsed time are as unsatisfactory as they are inaccurate, in both the acute and chronic cases, I have classed those cases as "chronic" in which there was no evidence of fresh or unhealed associated brain injury. Cases that still showed evidence of unhealed or acute brain injury have been classed as "acute subdural hematomas."

*Read by title at the annual meeting of the New England Surg. Soc. at New Haven, New Hampshire, September 5, 1941.
From the Department of Neurosurgery, Boston City Hospital.

†Assistant professor of neurosurgery, Harvard Medical School, Boston University School of Medicine, and surgeon in chief for neurosurgery, Boston City Hospital.

Since all hematomas are acute at the start and since they become chronic only because their presence has been unrecognized earlier by the attending surgeon, this distinction, although perhaps valid, seems to me to be unnecessary and artificial.

CHRONIC SOLID SUBDURAL HEMATOMAS

If the hematoma is formed of pure blood, such as that resulting from the rupture of a bridging vein, and if there is no tear in the arachnoid, the hematoma will be expansile only while the bleeding is unchecked. After the bleeding has stopped, the hematoma will clot, and the clot will be encapsulated between two membranes by the growth of fibro-

cause the other contents of the skull have been unable to accommodate themselves to this extra space-occupying lesion. This is the typical subdural hematoma associated with intracranial injury of the newborn² and is the type that develops from nontraumatic cases,—for example, in scurvy and blood dyscrasias,—as well as after craniocerebral injury. It is not necessarily an immediately fatal lesion even when associated with trauma. The patient is apt to have no significant symptoms at the time it is first formed, the injury is liable to be trivial, and the symptoms, when they do develop, are prone to be remissive. Until recently, clots that originated in trauma have usually been over-

TABLE I. Cerebral Intracranial and Cranial Complications.

TYPE OF LESION	CRANIAL INJURY			OTHER HEMORRHAGE			ACUTE CEREBRAL INJURY				CHRONIC CEREBRAL INJURY						
	SIM- PLE FRAC- TURE	DE- PRESSED FRAC- TURE	COM- FOUND FRAC- TURE	EX- TRA- DUR- AL	SUB- COR- TI- CAL	VEN- TRIC- ULAR	NONE	EDE- MA	CONTU- SION OR LACERA- TION	HY- PER- TENSIVE MIA	CON- VULSIVE SPIZURES	ADHIE- SIVE ARACH- NOID- ITIS	EN- CEPH- ALOP- ATITIS	OP- TIC NEU- RITIS	HY- PER- TENSIVE ROSIS	TOXIC DE- HYDRAT- ION	
Acute mixed subdural hematomas (194 cases)																	
Living patients	23	7	3	7	3	1	10	5	100	0	4	1	11				5
Dead patients	22	0	0	4	4	0	0	2	77	1	0	1	2				1
Totals	45	7	3	11	7	1	10	7	177	1	4	2	13	0	0		6
Chronic subdural hematomas																	
Fluid type (71 cases)																	
Living patients	2						67				14	3	9	1		3	
Dead patients	0						4				0	0	1	0		0	
Totals	2	0	0	0	0	0	71	0	0	0	14	3	10	1	3	0	
Solid type (45 cases)																	
Living patients	3						27				2	1	3	1			
Dead patients	0						15				3	0	4	0			
Totals	3	0	0	0	0	0	42	0	0	0	5	1	7	1	0		0
Both types (116 cases)																	
Living patients	5						94				16	4	12	2		3	
Dead patients	0						19				3	0	5	0		0	
Totals	5	0	0	0	0	0	113	0	0	0	19	4	17	2	3	0	

blasts on both the dural and arachnoidal surfaces, after which organization of the clot itself takes place from the two membranes. Depending on the relative speeds of organization of the surface and liquefaction of the center of the clot, the latter will be replaced by, at one extreme, a single fibrous sheet representing the fused membranes and organized intervening clot and, at the other, by a collection of fluid with a very high protein content contained entirely within membranous walls that are fibrous and may include calcium. The former is adherent to the dura, and even on microscopic examination may be indistinguishable from it except as a local thickening. The latter appears as a cyst with numerous vascular and fibrous adhesions between its wall and the dura, arachnoid and pia.^{10,11,15} It lies completely within the subdural space. Neither of these lesions is expanding. When they cause symptoms of increased intracranial pressure, they do so only be-

looked at the start and then recognized later only in the course of an investigation of the patient as a "brain-tumor suspect." This has been well emphasized by Horrax and Poppen.¹⁶ It is this group of subdural hematomas that, after having been overlooked and undiagnosed at their formation, have been discovered later and described as "chronic subdural hematomas." If the diagnosis has been even more inaccurate, the patients have been committed to insane hospitals as psychotic, only to have the true cause of their mental abnormalities first recognized at autopsy.¹⁷ This kind of clot was the subject of Putnam and Cushing's¹³ paper, and is the least common of all intracranial subdural hematomas.

Chronic solid subdural hematomas occurred forty-five times in this group of 310 verified cases (Table 1). In 3 cases, an associated diagnosis of "old contusion of the brain" could be made. However, in these, as well as in the other 42 cases, any associated

brain injury that had been present when the clot formed had long since healed by the time the hematoma had been diagnosed. Three cases had demonstrable fractures of the skull. Thirty-eight clots were solid and encapsulated, and seven were

only a trivial craniocerebral injury—many being unaccompanied by unconsciousness even—and the subsequent persistent but often intermittent headaches. Objective symptoms are minimal and, if present, are usually caused by the associated brain

TABLE 2 *Cause of Death*

TYPE OF LESION	CEREBRAL CONDITIONS		CIRCULATORY CONDITIONS			INFECTIONS					SURGICAL SHOCK	UNKNOWN
	MECHANICAL EDEMA	SYPHY TIFERNIA	CIRCULATORY FAILURE	ARTERIO SCLERO SIS	VASCULAR SYSTEM DYSFUNCTION	PNEU MONIA	SEPTIC EMIA	SEPTIC WOUND	SUBDURAL ABSCESS	EMPHY SEMA		
Acute mixed subdural hematomas	33	1	25	12	4	7	5	4	0	1	4	1
Chronic subdural hematomas												
Fluid type	0		2	0	0	2		0	0			
Solid type	4		8	3	1	2		2	1			
Both types	4	0	10	3	1	4	0	2	1	0	0	0

cystic and encapsulated, as described above. In 1 case, two solid clots were present. They were discrete, superimposed one on the other and both in the right parietal region. A fresh hematoma was present in addition to a chronic one—both being solid clots—in 1 case. In 1 case, the clot was calcified, and there was 1 in which simultaneous

damage and toxic dehydration. Later on, the subjective symptoms and signs are those of a brain tumor suspect. There is not necessarily any evidence of increased intracranial pressure. The diagnostic use of air in these so-called "chronic" cases by both the ventricular and lumbar subarachnoid routes has been recommended by Kun-

TABLE 3 *Location, Type and Identifiable Source of Clot*

TYPE OF LESION	LOCATION OF CLOT					TYPE OF CLOT							IDENTIFIABLE SOURCE OF BLEEDING	
	UNILAT ERIAL	BILAT ERIAL	CYRE ERIAL	PERE ERIAL	NOT KNOWN	AT CL R T	OLD AND NEW	MUL TI PLE	SOLID	CYSTIC	FLUID	CAL CI FIED	RUPTURED BRIDGING VEIN	PURTRUED VENOUS SINUS
Acute mixed subdural hematomas														
Living patients	75	10	110	0	0	4	5				21			0
Dead patients	58	14	77	1	1	4	2				4			2
Totals	133	33	191	1	2	8	7	0	0	0	25	0	0	2
Chronic subdural hematomas														
Fluid type														
Living patients			1								17			
Dead patients			4								4			
Totals	0	0	5	0	0		0	0	0	0	21	0	0	0
Solid type														
Living patients	13	7	30			1	1	1	26	4		0	0	
Dead patients	10	5	15			2	0	0	12	3		1	2	
Totals	23	12	45	0	0	3	1	1	38	7	0	1	2	0
Both types														
Living patients	13	7	97			1	1	1	26	4	67	0	0	
Dead patients	10	5	19			2	0	0	12	3	4	1	2	
Totals	23	12	116	0	0	3	1	1	38	7	71	1	2	0

right parietal, right occipital and right frontal clots were present, the parietal clot recurring after removal. A ruptured bridging vein was identified as the certain source of the clot in 2 cases. Both these patients died of circulatory failure and were autopsied, one having been operated on previously

kel and Dandy,¹⁸ Browder et al,⁵ Horrax and Poppen¹⁰ and, doubtless, many others. It is unquestionably of great and often indispensable aid. I have never approved either the need or the safety of its use in the acute phase, however, preferring bilateral transtemporal exploration.

Diagnosis

Early diagnosis of this type of hematoma depends on the recognition of a significant cause-and-effect relation between what may be considered

Treatment

Treatment is surgical, with removal of the solid, partially organized clot, and as much as is safe of the fused membrane that is the end result of com-

plete organization. Cysts should be emptied, and as much of the walls removed as is compatible with safety. In children, it is essential, as Ingraham and Heyl⁷ have shown, that the membrane, and especially the one that lies on the arachnoidal side of the clot, be fully removed if later stunting of the growth of the hemispheres is to be prevented. The operation, which should be done by way of a flap craniotomy, is apt to be bloody, and post-operative clots and severe cerebral edema are frequent complications.

Immediate Results

There were 15 deaths in this group of 45 cases — a mortality of 33 per cent. All except 1 patient were operated on. The causes of death are interesting (Table 2). Circulatory failure was the commonest. This was present nine times. Medullary edema was considered to be the cause of death in 3 cases, hydrocephalus in 1, a recurrent clot in 1, and lobar pneumonia in 1. The clots were present on the left, the right and bilaterally each five times. Two of the hematomas recurred after operation, and another was calcified. Twelve deaths occurred in the group of solid clots, and 3 in the cystic-clot group (Table 3). Two of the latter were the result of birth injuries, in one of which, no operation was performed, and the other was present in a man of sixty-seven. In this connection, it may be

group was twelve years less than that of the fatal cases — thirty-eight as compared with fifty years. It seems fair to conclude that the prognosis in the group of chronic solid cerebral subdural hematomas is altered to some extent by the age of the patient but not by any other specific factor. It is impossible to determine the rate of incidence of this class of cerebral subdural hematomas among craniocerebral injuries in general.

ACUTE MIXED SUBDURAL HEMATOMAS

When both blood and cerebrospinal fluid collect and mix in the intracranial subdural space, the appearance of the resulting clot varies within wide limits. Macerated cortical tissue may also be added to the mixture. If the blood is at a maximum and the cerebrospinal fluid at a minimum, the clot closely resembles that described above as an "acute solid hematoma" — the variation being chiefly in the length of time that elapses before the blood solidifies. If, on the other hand, there is a maximum of cerebrospinal fluid, and a minimum of blood, the mixture and subsequent solution of the latter in the former preclude all attempts on the part of the dura to organize the hematoma. The hematoma is represented, therefore, by a collection of pigmented fluid with a high protein content. It is incarcerated in the subdural space but is, nevertheless, free to move anywhere within that space. It requires no great stretch of the imagination to visualize the change that variations in the relative concentration of blood and cerebrospinal fluid might make in color, consistence, and rate and completeness of coagulation in this type of hematoma. So long as coagulation and, therefore, organization by encapsulation do not take place, this blood dissolves in the cerebrospinal fluid that has escaped into the subdural space. This solution is separated by a dialyzing membrane — the arachnoid — from another solution (the cerebrospinal fluid) that has a relatively low protein content and a low osmotic pressure in relation to the hematoma. Under such circumstances, osmosis, with migration of the fluid of low protein content across the membrane to, and consequent dilution of, the solution of high protein content, is inevitable. With this movement and as the direct result of it, there is of necessity an increase in the amount of the high protein solution. This type of subdural hematoma is therefore an expanding lesion during the periods of solution and osmosis. The rate of expansion, which is rapid for the first five weeks, gradually decreases over the next two months as the concentration of protein in the two solutions approaches equality. This sequence of events has been demonstrated experimentally by Gardner¹⁴ and by a graphic study of eighty-nine such fluids by Munro.² Browder et al.⁵ consider my "theoretic explanation

TABLE 4. *Age Groups.*

TYPE OF LESION	YOUNGEST	OLDEST	AVERAGE	NUMBER OF PATIENTS
Acute mixed subdural hematomas				
Living patients	4 months	68 years	40 years	115
Dead patients	11 months	77 years	50 years	79
All patients			44 years	194
Chronic subdural hematomas				
Fluid type				
Living patients	5 months	62 years	30 years	67
Dead patients	8½ years	5 years	31 years	4
All patients			30 years	71
Solid type				
Living patients	9 weeks	66 years	38 years	30
Dead patients	10 months	67 years	50 years	15
All patients			42 years	45
Both types				
Living patients	9 weeks	66 years	38 years	97
Dead patients	10 months	67 years	40.5 years	19
All patients			40.5 years	116

noted that the average age of this group of fatal cases was fifty years, the youngest being ten months and the oldest sixty-seven years (Table 4).

All the 30 living patients had been operated on. Ten clots were on the left side, thirteen on the right, and seven bilateral. One recurred and was removed at the second operation (Table 3). Although the youngest patient was nine weeks and the oldest sixty-six years of age, the average age of this

that a subdural hematoma may be augmented by osmosis in a certain number of such lesions" entirely logical. They find it difficult, however, to explain certain variations in the consistence and color of different clots that have been present the same length of time after the injury. This finding has been my experience also, but unlike them I find no difficulty in accepting the explanation that, although the time interval is the same, the relative amounts of blood, cerebrospinal fluid and cortex are highly individual and should therefore produce hematomas in two of which can be alike.

This mixed type of subdural hematoma occurs exclusively as the result of craniocerebral injuries. In addition to damage to blood vessels on the brain surface, there is always a tear in the arachnoid. Thus, as noted above, in addition to blood, cerebrospinal fluid is discharged in varying amounts into the subdural space. The blood is commonly from cortical veins, less often from the large venous sinuses and less often still from cortical arteries. I have never seen the latter, but Browder and his associates⁶ report its occurrence. If the injury has produced a laceration of the pia and the brain, cortical tissue may also be added to the blood and cerebrospinal fluid. Since these patients have, as a rule, severe brain injuries in addition to their hematomas, since many of them are in surgical shock for a varying period after the receipt of the injury and since these hematomas are expanding lesions, there is an associated compression of the brain that is beyond that which may be produced by uncomplicated cerebral injury. This group of patients has the highest fatality rate. In general, they are the ones who are first treated for a lacerated or contused brain but who despite that therapy get worse and often die with the clot unoperated on and undiagnosed. The prognosis is not invariably fatal, however, even in the absence of active therapy. Many patients, especially those whose hematomas contain less rather than more blood in relation to the amount of cerebrospinal fluid, recover from the immediate effects to become chronic invalids until such time as their fluid subdural hematomas or, as many are improperly called, their "hydromas" are removed. Early diagnosis and early treatment of the mixed subdural hematomas obviate this difficulty and save many lives in addition. It is this mixed type of subdural hematoma that is far and away the commonest of the subdural clots. If real progress is to be made in the reduction of the immediate mortality of craniocerebral injuries and the elimination of later disabling post traumatic neuroses and invalidism, the attention of the medical profession must be concentrated on this group of cases to a much greater degree than it has been in the past.

In this group of 310 cases, 194 had acute mixed subdural hematomas. These were complicated by a recognized associated major brain injury in 184 cases. Its presence was verified at operation or autopsy in every case. No note of any brain injury was made in the other 10 cases. A fracture of the skull was demonstrated in 55. Forty five of these were simple, seven were depressed, and three were compound fractures. Nineteen cases had other major complicating hemorrhages. Eleven were extradural, seven subcortical, and one ventricular. Toxic dehydration was present in 6 cases. No clots could be traced to ruptured bridging veins (Table 1). Six patients had infected wounds.

Diagnosis

I am convinced that a certain diagnosis of the presence of a mixed subdural hematoma can be made only by exploratory trephination. The next most accurate method is by either an encephalogram or a ventriculogram. I consider an encephalogram too dangerous a method to be used in these acute cases, and mention it only to condemn it. I see little to choose between the risk of a ventriculogram and an exploratory trephination. Since my experience leads me to believe that explorations made in areas other than the temporal miss a certain percentage of temporal and frontal clots and since exploration together with ventriculography forces the operator to make biparietal or bifrontal trephines, I have never felt justified in using air in this way in these cases. Aside from the operative demonstration of a subdural collection of blood, the most important diagnostic aid is to recognize the presence of a brain injury, treat it adequately, and then be prepared to carry out a transtemporal exploration if the patient fails to improve or gets worse under nonoperative therapy. Of course, before exploration, toxic dehydration must also be eliminated as a cause of the continued symptoms. The subjective and objective symptoms produced by these hematomas cannot be distinguished from those caused by either an uncomplicated brain injury or toxic dehydration. Lateralizing signs are notoriously inaccurate. The cerebrospinal fluid is altered from normal only because of the brain injury, and its pressure may be high, normal or low, even in the presence of a large clot. I have not seen any dependable regularity in the development of coma or a latent interval and do not regard their presence or absence as being of any diagnostic import. I have the impression that lasting mental changes and the development of a contralateral central facial palsy while the patient is under treatment are commoner in the presence of mixed subdural hematomas. Unilateral fixed dilatation of the pupil is a suggestive

diagnostic sign, but it is not reliable.¹ Exploratory trephination, transtemporal by preference and bilateral if necessary, is never contraindicated in a patient who has been knocked unconscious by a blow on the head and who is not getting better or is getting worse under adequate lumbar-puncture and fluid therapy.

Treatment

Just as in the cases of solid hematoma, the treatment of the acute mixed hematoma is exclusively surgical. The operation should not be done while the patient is in shock or toxic from dehydration, but otherwise should be carried out in accordance with the requirements noted above. When a hematoma is found and no matter what its physical consistence may be, it should be removed by suction as completely as possible after the majority of the squama and the adjoining edges of frontal and parietal bones have been removed and the dura opened to the limit of the bony windows. Afterward, the subdural space should be drained with rubber tissue and the dura left open. The rest of the wound should be closed in layers. Irrigation of the damaged cortex should be studiously avoided. The approach should be through a vertical muscle-splitting temporal incision. I consider bone flaps contraindicated and too dangerous. It should be noted, however, that Browder and his associates⁵ advise and use small bone flaps with apparent satisfaction and success in this type of case. The postoperative care of these patients requires as much judgment and skill as the operative procedure—indeed, more in many cases. The brain injury must be treated, and in addition, the need for intelligent general supportive measures is more than ordinary. Finally, malignant postoperative edema is very prone to develop and unless treated with all the means at one's command will bring about a fatal ending to an otherwise successful case.

Immediate Results

Seventy-nine of the 194 patients with acute mixed subdural hematomas died in the hospital. This is a mortality of 41 per cent. Since all patients were operated on, the operative mortality is essentially the same. The causes of death in the fatal cases are interesting and particularly so when compared with the cause of death in the fatal cases of solid hematoma (Table 2). Circulatory failure was again the chief cause, having occurred in 29 cases. Next, came medullary edema, with 27. Pneumonia and meningitis caused 5 and 6 deaths respectively; in 4 of the 6 cases with meningeal infections, the complication occurred postoperatively. Surgical shock caused 4 deaths, recurrent un-

recognized clots, 2, and respiratory obstruction, uremia and empyema thoracis, 1 each. In 1 case, the cause of death was not clear. Eleven patients died without operation. All were autopsied, and the cause of death determined thereby. Fifty-eight clots were unilateral, twenty-eight being on the right and thirty on the left. Fourteen were bilateral, four recurred, and 2 patients had a combination of old and new clots. There were no multiple clots. Four hematomas were fluid as distinct from the liquid and solid clots in that there was no gross solid material present. Seventy-six were cerebral, one was cerebellar, and the location of two was not given (Table 3). The youngest of the patients who died was eleven months, the oldest seventy-seven years, and the average age was fifty years. In 3 cases, the age was not known (Table 4). The immediate effects of the operative procedure, as represented by medullary edema, postoperative infections and circulatory incompetence, were major factors in determining the number of fatalities. Of these, the last is the only one with prognostic significance under the circumstances and, when taken in conjunction with the ten years' difference in the average age of the fatal and nonfatal groups, emphasizes again that the older the patient with a subdural hematoma, the worse the prognosis.

One hundred and fifteen patients with acute mixed subdural hematomas survived and left the hospital relieved of the symptoms that brought them in. In 75, the clot was unilateral, forty-one being on the right and thirty-four on the left. Nineteen were bilateral. In 5 cases, both old and new hematomas were present. In 1, they were bilateral—that is, four clots; in 1, one clot was on the right and the other on the left; in 1, both clots were on the right; in 1, both were on the left; and in 1, a fluid clot was present in association with a solid right-sided hematoma. Four clots recurred after operation—one bilaterally and three on the right side. Twenty-one were fluid in type, being unlimited in their freedom of movement within the cerebral subdural space. The total protein in 14 of these and in 2 of the 4 similar fatal cases ranged from 4020 to 56 mg. per 100 cc., with an average of 396 mg. In 3, the fluid clotted before it could be examined. All one hundred and fifteen hematomas were cerebral (Table 3). As in the group of solid hematomas, the average age—forty years—was ten years less than that of the corresponding patients who died. The youngest patient was four months, and the oldest sixty-eight years (Table 4).

CHRONIC FLUID SUBDURAL HEMATOMAS

When the fluid type of mixed subdural hematoma—that is, the type made up of a maximum

of cerebrospinal fluid and a minimum of blood—is allowed to go untreated until after the acute brain injury is healed, it may be said to have become chronic. This is in accordance with the definition of chronicity as given above. Depending on its size, the amount of dissolved blood, the percentage of protein originally contained within it and the length of time that has elapsed between its formation and its discovery or operative removal, it may still be either an expanding lesion and increasing in amount or fixed in relation to both its protein content and its size. In either event, it will be, as it has been from the beginning, incarcerated within the subdural space but free to move anywhere within those limits. I¹ have described these hematomas in detail elsewhere and need not repeat the description here. Others have also described them, but, in my opinion, incorrectly—as “hydromas.” Hydroma or hygroma is defined as a ‘sac, cyst or bursa distended with a fluid’.¹⁰ This term is therefore only descriptive and carries no pathological significance. The term was first applied to subdural fluid accumulations by Naffziger,²¹ before the problem of subdural hematomas was understood. Its continued use, as advocated by da Costa and Adson²² in the mistaken belief that a hydroma is a separate entity and not one form of subdural hematoma, is not justified. Their failure to explain how air put into the subarachnoid space can reach the subdural space and outline fluid therein *after* the tear in the arachnoid has closed and incarcerated the fluid, and particularly when the latter is enclosed within cyst walls as well, is a fatal omission. There seems to me to be a need for a clearer understanding of the entire subdural hematoma problem rather than for the identification of another pathological entity.

Suffice it to say that, just as with the chronic solid clots, so these chronic fluid clots would not exist had their presence been suspected and verified at the time of the original craniocerebral injury, because they are all the direct result of such injuries. This extremely disabling but nonfatal condition is always caused by an injury to the head. The symptoms are those commonly described as being caused by post-traumatic neurosis or malingering, and are usually associated with a severe and persistent true neurosis. If untreated, the patients become hypochondriacal invalids and permanent charges on the community. They do not go insane, nor do they die as the result of this condition.

This type of hematoma occurred in 71 of the group of 310 patients. None had any associated brain injury at the time of examination, although it was possible to demonstrate a simple fracture of the skull in 2 cases. Complications that were frequent in the other types of subdural hematomas

were conspicuous by their absence. On the other hand, there was an unduly large preponderance of the type of condition that suggests permanent brain damage. For example, 14 cases had convulsive seizures, 10 had intellectual changes classified as “encephalopathy,” 1 had optic neuritis, and 3 had hysteroneuroses (Table 1).

Diagnosis

A correct diagnosis can be made only at operation. Air injection is of no help, as has been shown by von Storch and Munro.²³ The cerebrospinal fluid is normal, as is the intracranial pressure. Objective and subjective signs and symptoms are conspicuous by their absence—their presence being significant from a prognostic rather than a diagnostic point of view, the occurrence of convulsive seizures being especially unfavorable. In general, the statements made in this regard in an earlier paper¹⁰ still hold true.

Treatment

The treatment is surgical. The operation should be done as soon as possible after the receipt of the injury, since the shorter this interval the greater the chance for a permanent cure. The subdural space should be exposed through a transtemporal approach, as described above. The approach need be only on one side, preferably that opposite the speech cortex. As much as possible of the fluid hematoma should be removed, and the subdural space drained with rubber tissue. The wound is closed in layers except for the dura, which should be left open. There are usually no postoperative complications, and the patients have immediate and permanent relief so far as their associated neurosis and permanent cerebral changes allow.

Immediate Results

Four of these 71 patients died—2 of lobar pneumonia, 1 of progressive encephalomalacia and circulatory failure, and 1 of heart failure and chronic alcoholism (Table 2). Their ages were forty three, fifty nine, eight and a half and fifty five years respectively—an average age of thirty-one years (Table 4).

Sixty-seven patients survived. Eight were not relieved of the symptoms for which they had been operated on. The youngest was five months, and the oldest sixty-two years, the average age being thirty years (Table 4). For what they are worth, the comparative figures demonstrate that in this type of hematoma, age has little effect on prognosis so far as mortality is concerned.

DISCUSSION

This series of 310 major subdural hematomas demonstrates that no less than 62 per cent of intracranial subdural hematomas can be recognized

in their acute stage. If they are so recognized, the mortality can be expected to be in the neighborhood of 40 per cent.^{5, 24} It varies with the patient's age and the efficiency of his circulation. So far as the individual types of hematomas go, the fatalities show a consistently higher age level. It seems reasonable to conclude that increasing age is a detriment to the patient in the acute phase of this disease but has little influence on the mortality when the chronic forms are considered. The

lished.² The incidence in this particular group is 13 per cent, but my series is undoubtedly "loaded" because serious and operable cases gravitate toward and mild and nonoperative cases away from my service. I cannot account for the discrepancy between these figures and the 1 per cent incidence reported by Browder et al.⁵ My mortality, on the other hand, is essentially identical with his—41 per cent. In my series, of course, this refers only to the acute mixed

TABLE 5. *Miscellaneous Complications.*

TYPE OF LESION	CIRCULATORY CONDITIONS			INFECTIONS					OTHER INJURIES			GENERAL CONDITIONS			MISCELLANEOUS CONDITIONS	
	ARTERIO-SCLEROSIS	VASCULAR HYPERTENSION	HEART DISEASE	PNEUMONIA	EMBOLISM	SEPTIC WOUND	NEPHRITIS	OSTEOMYELITIS OF THE SPINE	FRAGILE PELVIS	FRAGILE SPINE	PUPPATED SPLEEN	ALCOHOLISM	SYPHILIS	AVITAMINOSIS	BRAIN TUMOR	CHORIORETINITIS
Acute mixed subdural hematomas																
Living patients	9	1	2	6	1	2	0	1	1	1	0	10	2	1		
Dead patients	12	4	0	7	1	4	2	0	0	0	1	6	2	0		
Totals	21	5	2	13	2	6	2	1	1	1	1	16	4	1	0	0
Chronic subdural hematomas																
Fluid type																
Living patients	1			0								1			1	
Dead patients	0			2								1			0	
Totals	1	0	0	2	0	0	0	0	0	0	0	2	0	0	1	0
Solid type																
Living patients	1	1	2	0		0						1	0		1	1
Dead patients	3	1	0	2		2						0	2		0	0
Totals	4	2	2	2	0	2	0	0	0	0	0	1	2	0	1	1
Both types																
Living patients	2	1	2	0		0						2	0		2	1
Dead patients	3	1	0	4		2						1	2		0	0
Totals	5	2	2	4	0	2	0	0	0	0	0	3	2	0	2	1

additional prognostic significance of inefficiency of the circulation is of equal importance. This is only too evident from the figures in Table 2 and particularly so if one adopts the broad point of view, which recognizes that medullary edema and hyperthermia are at least closely linked to changes in the circulation.

Miscellaneous complications occurring in this series are listed in Table 5. They are of no great significance except so far as alcoholism and syphilis are concerned. As is well known, both syphilis and alcoholism have been held to be major if not exclusive causes of cerebral subdural hematomas. This series demonstrates conclusively that their presence is merely coincidental. Their single possible etiologic connection has to do with alcoholism, and this is recognizable only because a person who is drunk is likelier to injure his head than a sober one.

Cerebral subdural hematomas may be expected to occur in about 10 per cent of all hospitalized craniocerebral injuries. This incidence is considerably less than the figures I have previously pub-

hematomas and predicates a willingness to do early and frequent diagnostic transtemporal trephinations.

No attempt has been made to determine the details of the causative accidents or the sex of the patient. An unrecognized and improperly treated subdural hematoma is as fatal in a woman as it is in a man, and it is of little moment, so far as diagnosis and prognosis are concerned, whether it followed an automobile accident, a kick by a horse or a fall from a window. The important thing is to treat the condition early and adequately, and thereby reduce to a minimum the so-called "chronic" hematomas with their associated disabling symptomatology and at the same time lower the mortality of the acute cases.

CONCLUSIONS

In general, it is undoubtedly true that the commonest intracranial subdural hematoma is the mixed type and that the cause for its formation is trauma to the head. The presence of a cerebral subdural hematoma, regardless of its variety, does

not necessarily lead to a fatality. When the patient survives the immediate effect of the injury, the hematomas inevitably cause later symptoms. These symptoms will be disabling, interfere with the economic efficiency of the patient, and lead to a permanent neurosis, which may be associated with permanent structural changes in the brain. Such tragic late effects are preventable if the physician who sees the patient at the time of the original craniocerebral trauma bears in mind the fact that if patients with only contusion and laceration of the brain are adequately and promptly treated they will get better and be freed of their major symptoms rapidly. If such patients fail to get better, or get worse, however, the responsibility rests with the physician to recognize the possibility that a mistake has been made in the diagnosis and that, as a result, he must investigate and treat the cause of this failure to recover by every means at his command.

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INSTRUCTION OF LAYMEN IN THE EMERGENCY SPLITTING OF FRACTURES

BOARDMAN M BOSWORTH, MD*

NEW YORK CITY

ACCIDENTS do not happen at carefully chosen sites. They are apt to occur under conditions in which medical aid either cannot be obtained or can be had only after a prohibitive lapse of time. Such accidents take place in the woods or fields incidental to hunting and sports, or on highways in thinly settled districts. There is now the added possibility of large scale public disaster, explosion, bombing or invasion in which medical facilities, although immediately available, are temporarily overwhelmed.

The present state of national emergency has stimulated in the general public an unprecedented interest in the handling of accidental injuries, an interest that is well attested by recent dramatizations of first aid treatment in popular magazines. In the past, lay education along these lines has been neglected by the medical profession, with the exception of certain relatively small select groups, such as the Red Cross and Boy Scouts. Now

comes a sudden demand on instruction of civilian defense splitting of emergency injuries must be met and is being met by the country, who are out of time and energy, chiefly by the American Red Cross lay groups in the emergency.

To many a physician seem new and strange enthusiasm and will with thorough master with some knowledge of physics, specialist of learning, trained to positive memory, is presented to them the instructor must avoid other pitfalls, effectiveness the

*Assistant surgeon, New York City Hospital; assistant surgeon, Outpatient Department, St. Luke's Hospital; surgeon, Outpatient Department, New York Hospital.

Use simple language—burden your audience with as few technical terms as possible.

Repeat, and repeat again, a few essentials—do not try to cover a mass of details.

Emphasize basic principles so that the student will understand clearly what it is that he is trying to do.

In choosing among several methods of first-aid treatment, present only the simplest effective one.

Be practical—present actual in preference to hypothetical cases, and confine yourself to the real limitations of the case presented and be sure that the method described can be used in the situation under consideration.

Since fractures make up a great part of all accidental injuries, the problem of giving instruction in emergency splinting naturally assumes considerable importance. At first glance, the subject of splinting seems to be an easy one to teach. But as one examines it more closely, certain difficulties

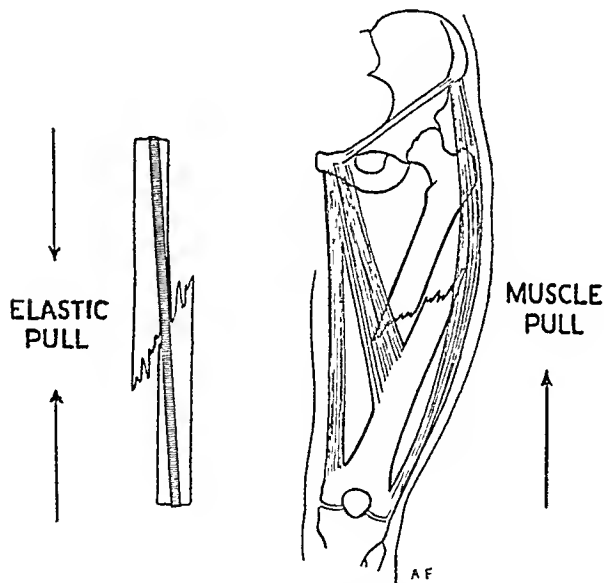


FIGURE 1. *The Pull of a Rubber Band over the Ends of a Broken Stick Illustrates Muscle Pull on a Broken Bone.*

appear. The rationale of splinting is, of course, simple to explain. The pull of a rubber band over the ends of a broken stick suggests the effect of muscle pull on a broken bone (Fig. 1). The rubber band causes each fragment of the stick to slip past the other; with a broken bone, on the other hand, the proximal end is fixed by the body so that the distal fragment tends to be drawn past the proximal. The potential damage to soft tissues by the knifelike ends of bone fragments that have not been splinted can be readily demonstrated, as can the salutary effect of a properly applied splint (Fig. 2). But, presumably, the layman will have no Thomas, Murray-Jones or Keller-Blake splint

available, nor will he have at hand an adequate supply of flannel, muslin and gauze bandages, basswood splints, tongue blades, safety pins, rope and adhesive tape. What can he do?

It is no answer to urge that first-aid kits and splints be carried in every car and kept in every home. This worth-while objective may some day become a reality, but for the present it will not solve the first-aid worker's problem. Instead, he must be

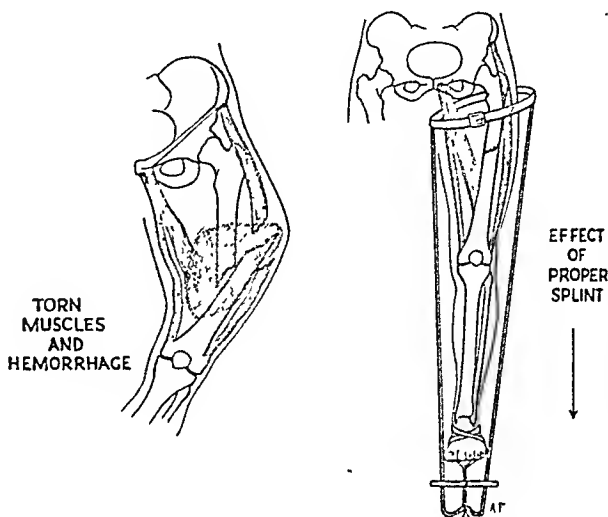


FIGURE 2. *Soft-Tissue Damage Resulting from Transportation without Splinting Compared with Bone Fragments Controlled by an Adequate Splint.*

shown that these materials, although desirable, are by no means essential and that adequate splinting can be achieved quite simply and effectively by using such things as may be at hand or close by. In short, he must be taught to improvise. This calls for ingenuity and imagination in the instructor quite as much as proficiency in technic and experience in teaching.

During the last six months, under the auspices of the New York and Brooklyn Regional Fracture Committee of the American College of Surgeons, a motion picture in color, demonstrating for the layman the emergency splinting of fractured arms, legs and spines, has been produced.* The film is designed to show how an effective splint can be improvised and applied by anyone in a few moments, under emergency conditions, only materials ordinarily available near the scene of an accident being used. The experience gained during the production of this picture may be helpful to others who have volunteered to teach first aid for fractures.

The methods of splinting described below are not necessarily the best, but they have been tested

*"Splint 'Em Where They Lie!" A 16-mm. Kodachrome motion picture in two parts. Part I: Fractures of the extremities (400 feet). Part II: Fractures of the spine (200 feet). The films may be obtained, through the author of this paper, for exhibition to lay or professional groups.

and found effective. Above all, they have one outstanding virtue: they are extremely simple, easily taught and well remembered. Modifications and improvements will undoubtedly occur to many. Certainly, no claim to originality is made. Rather, the basic idea throughout is to suggest what may be used for splinting and thus to stimulate the imagination and originality of others. The following description of emergency fracture care is an outline of the subject in a form suitable for presentation to lay groups.

DIAGNOSIS

The first task the physician instructor has to face is teaching diagnosis. In most cases, the layman cannot be expected to know whether or not a fracture is present unless he makes some kind of examination. Besides, the victim may be unconscious or drunk, or too badly frightened, be wildered or hysterical to co-operate intelligently. More significant is the fact that an examination may disclose the presence of other fractures, which might easily be overlooked in the enthusiasm and excitement of getting to work on the victim. It is only natural for the novice to concentrate his attention on an obviously broken arm or leg, unaware that the victim has also sustained the far more serious injury of a fractured spine. The possible dire consequences of such an error can well be imagined. The layman must therefore be taught some simple but thorough method of examination, and the instructor should insist that he apply it before undertaking first aid measures as such. Rarely do conditions justify a reversal of this procedure.

What should the examination include, and how comprehensive should it be? Specifically, just what should the layman be trained to look for? In fractures of the extremities, certain cardinal signs, such as local pain, tenderness, loss of function and gross deformity, are readily determined. Search for them can do the victim no harm, and their presence should at least make the layman suspect a fracture. He should also be taught that the peculiar grating sensation, known as crepitus, produced by broken bone fragments, and abnormal freedom of motion in one extremity compared with the opposite are major signs that are present in many fractures. But, at the same time, he must be strictly cautioned that many fractures exhibit neither the one nor the other and that attempts to elicit them are not only unnecessary but are to be severely condemned as being apt to do much harm.

Fractures of the spine often present special difficulties in diagnosis, even for the trained physician. Any great degree of accuracy in their recognition by laymen, therefore, is not to be ex-

pected. Local pain, tenderness and disability are inconstant and unreliable. Paralysis or anesthesia of the extremities, or both, if present, are significant but must by no means be considered essential for a diagnosis. After these facts have been pointed out to the layman, it is well to stress the value of treating as an actual spine fracture any injury to the neck or back that presents one or more of the signs mentioned above.

The layman must be taught the necessity of recognizing shock early and of becoming thoroughly familiar with its ordinary manifestations: pallor, weakness, faintness, cold clammy extremities, weak pulse and shallow respirations. He should approach the problem of diagnosis calmly and with assurance. He must take what time is necessary for a thorough and systematic, but gentle, examination. This is far more easily said than done at the scene of an actual accident. The volunteer is often subject to interference by anxious relatives and importunate bystanders, who demand action of some kind immediately and deprecate his efforts to ascertain first the nature and extent of the victim's injuries. The first aid worker must not allow himself to become disconcerted by this well meant but unfortunate pressure. He must proceed deliberately in spite of it until he has concluded a satisfactory examination and determined the number, kind and severity of the injuries present.

FIRST AID CARE

Fractures in General

The general condition of the victim of an accident should receive first attention. Following a major fracture, a person may or may not be in great pain; however, he is practically always suffering from some degree of shock, and simple measures to combat this condition should promptly be initiated. Among these may be mentioned covering the victim with coats or blankets to preserve body warmth. The administration of mild stimulants, such as hot coffee and tea, although advantageous, is usually impracticable under the circumstances of the accident. If the victim is kept warm from the outset, however, much will have been accomplished. In addition, splinting and immobilization of the fracture will, of themselves, tend still further to reduce shock. Active bleeding must, of course, be controlled at once, but this is a separate subject and lies outside the scope of the present discussion.

Regarding the emergency handling of compound fractures, physicians themselves are not agreed. My own conviction is that the layman should be taught the difference between a compound and a simple fracture and the reasons, chiefly potential contam-

ination and infection, for the greater seriousness of the former. He can also be shown the risk of converting a simple into a compound fracture by transporting the victim without proper splinting (Fig. 2). As a matter of practical expediency, I believe he should be taught to apply a traction splint to any fracture of a major extremity, simple or compound, before attempting to move the victim.

Fractures of Extremities

In a fracture of an arm or leg, while one person is concerning himself with the general condition of the victim, another should steady the fractured extremity. He should stay with the victim and continue the support while others seek a suitable splint. Material that will serve as a splint is usually the most difficult part of the required equip-

Application of the splint is a relatively simple matter. In place of bandages, rope and adhesive, various articles of clothing can be used effectively. For example, if an old board is used to splint a fractured thigh, it can be applied as follows (Fig. 3). A coat is slipped between the victim's thighs with the neck of the coat toward the crotch, and a loop is loosely fashioned about the upper portion of the hip by knotting the ends of the sleeves together. A folded hat is placed between coat and crotch to ease pressure against the latter when the splint is tightened. The upper end of the board is then engaged in the loop formed by the coatsleeves. At this point, a smooth, steady pull is exerted on the foot by the assistant, who has been steadying the injured extremity. This pull, once begun, must never be relaxed until the splint has been applied and finally adjusted.

Two neckties, knotted together to form one tie of double length, are looped over the ankle, which has been padded with another folded hat or other thick material. The neckties are then passed along each side of the foot and over the lower end of the splint, where they are tied tightly together. The loop thus formed is tightened by means of a small stick passed through it and twisted over and over. The stick is kept from untwisting by a handkerchief tied around it and the splint. The necktie loop should be tightened in this manner until the broken bone is steadied. Further tightening beyond this point is not only useless but dangerous to the circulation. Thus, traction, or pull, has been provided to overcome muscle spasm, but this is not enough.

The thigh and leg must be wrapped securely to the splint to support the extremity and prevent motion of the broken bone. The rest of the coat, whose sleeves are serving as a traction loop, is wrapped snugly about the thigh and splint. Garters, suspenders or neckties are passed around it and fastened for additional support. In similar fashion, the leg is wrapped to the splint, a vest, shirt or another coat being used. The splinted leg may then be lowered, but one must keep the heel of the foot off the ground by resting the lower end of the splint on a stone or other support. This avoids painful and dangerous motion of the bone fragments. It should be emphasized that only then is the fracture victim ready to be moved from where he has fallen. When the victim is picked up, the foot of the injured extremity should never be lifted; one should always lift the splint by which it is supported. Similarly, when the victim is placed in a car for transportation, a support for the end of the splint is arranged so that the foot hangs free, suspended by the splint. These simple precautions greatly minimize pain and shock.

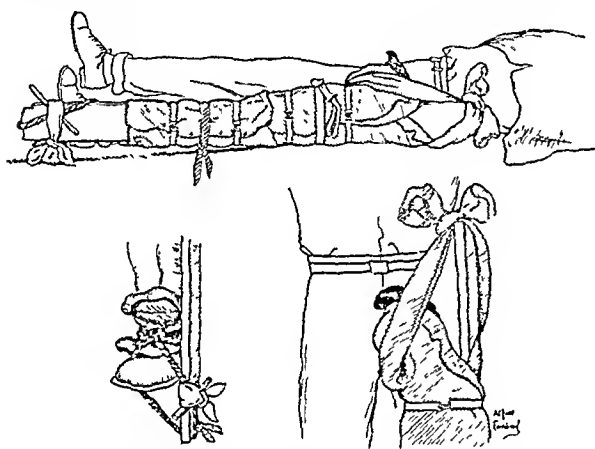


FIGURE 3. *Emergency Splint for Fractured Thigh or Leg, Improvised with an Old Board and Articles of Clothing.*

ment to improvise under emergency conditions, and yet at times it may be surprisingly easy. A fence rail, signpost, fallen tree, broom, rake, rifle, skipole or ski is adequate, and other materials may suggest themselves. Under certain conditions, such as darkness, storm and freezing cold, more harm than good may result from the delay caused by seeking a splint, and it may be much wiser simply to bind one leg to the other or the arm to the body than to run the risk of increased delay and exposure to a seriously injured and weakened person. Each case must be considered on its merits, and if there is any real question between life and limb, the issue must, of course, be decided in favor of the former.

Ideally, the splint should be light but strong. It must be of sufficient length to reach from above the shoulder to well below the hand in a patient with a broken arm, or from above the hip to considerably below the foot in one with a fractured thigh or leg. It is much better for the splint to be too long than too short.

A broken arm can be provided with an emergency splint in much the same way (Fig. 4). One assistant steadies the arm by taking a firm grasp of the hand. Pull on the arm must not be so strong as pull on the leg, since the muscles are weaker. A coat is slipped between the arm and



FIGURE 4. Broken Arm in Emergency Broom Splint.

Note that a coat is thrown over the body to keep the victim warm.

the body, and its sleeves are looped above the shoulder, as described above. A folded hat or other pad is placed in the armpit to relieve pressure, and the upper end of the improvised splint is engaged in the coatsleeve loop. Neckties, looped over the wrist, which has been padded with another folded hat, are tied over the lower end of the splint and tightened with a small stick just sufficiently to steady the bones.* The stick is again held in place with a handkerchief tie, and another handkerchief, loosely tied about the splint, gives the hand support. The arm and forearm are then

wrapped to the splint exactly as in the treatment of a broken thigh.

Fractures of the Spine

When one presents this part of the subject, it is well to make sure that the layman understands clearly what the spine is, in general how it is constructed, and what purposes it serves. He should be shown, with a rough sketch or two, that it is made up of a number of small blocks of bone, of more or less equal size and shape, placed one on top of another in a tall column (Fig. 5). The instructor should point out that the function of the

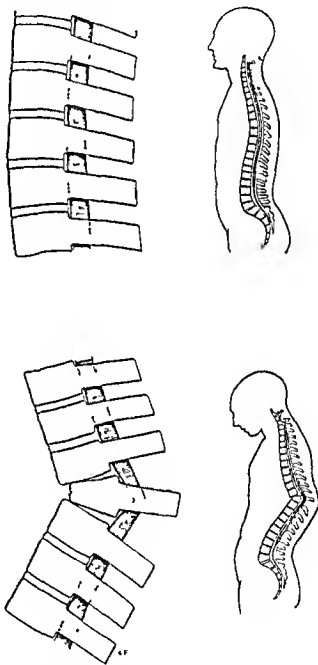


FIGURE 5 Anatomy of the Spine and Cord, Simplified to Show the Mechanics of a Fracture of the Spine.

spine is not only to support the body but also to protect a large bundle of vital nerves—the spinal cord—that connect the brain with the rest of the body. This should be sufficient anatomy. Any attempt to give it in more detail will confuse the listener and interfere with a clear grasp of the subject. After all, time, as well as the average mental capacity, is limited.

Having laid this groundwork, one should explain the mechanics of injury. Sudden, violent for-

*It must be emphasized in no uncertain terms to a lay group that major blood vessels and nerves lie close to the surface in the armpit where they are extremely vulnerable to pressure. Not only must the armpit be well protected with padding but also great care must be taken not to apply excessive traction by turning the small stick up too tightly. Paralysis resulting from overpull is a real danger that must not be forgotten. Pull should not exceed 4 or 5 pounds and when there is doubt, it is far better to have the Spanish windlass too loose than too tight.

ward bending of the spine, as in a fall from a height or in an automobile collision, should be stressed as the usual cause of such fractures. The possibility of damage to the cord should be given as sufficient reason for treating any suspected back injury as a fractured spine, and forward bending of the spine, during handling of the victim, should be avoided for the same reason.

Concerning the exact method the layman should be taught in dealing with a suspected spinal

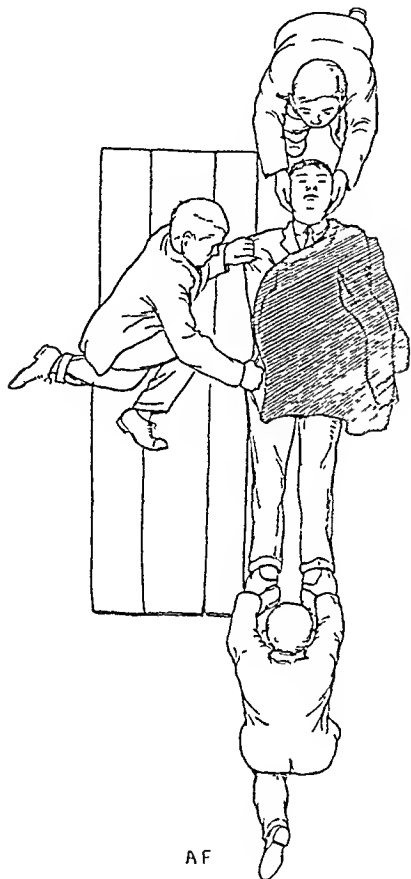


FIGURE 6. *Method of Moving a Victim with a Fracture of the Neck to an Improvised Stretcher.*

injury, there is room for some difference of opinion. Although details may vary, the underlying principles remain the same. Here again, in my opinion, simplicity should govern. After the victim's general condition has received attention, some strong flat support on which to place him must be found. This may be a board, shutter, door or other large flat object. It should be nearly body length or longer. Securing an adequate support of this kind often proves difficult, and it may be necessary to go some distance to find anything that will serve. Weather and the victim's general condition permitting, however, the effort should be made. Transportation of these injuries without proper support is extremely hazardous.

When the neck is injured, one person kneels facing the top of the victim's head and, grasping the sides of the face and jaw between his hands, steadies the head in line with the body (Fig. 6). No pull should be made on the head, and care must be taken not to bend the neck forward. An assistant supports the legs by holding the feet. A third helper then reaches across the door or other support that has been placed beside the victim and takes a firm grasp of the clothing at hip and shoulder. At a given signal, the victim is slid sidewise onto the door. All assistants must work smoothly together so as not to twist or bend the victim's neck. Support of the head must not be relinquished once the victim has been placed on the improvised stretcher but must be maintained throughout transportation. The door, with the injured person on it, may then be lifted and placed in a truck or wagon for conveyance to a hospital.

When the back is injured and the victim lies face down, he may simply be pulled sidewise onto the door by two people working together, one grasping the feet and the other the clothes at hip and shoulder, as described above. If the victim happens to lie face up, his arms should be brought above his head, and he should be rolled slowly over on the door, which has been placed on the ground alongside him. When this is done, it is essential to keep the trunk and extremities in line so that they are moved as one piece. In this way, the victim's back is not twisted or bent, and danger to the spinal cord is avoided.

When a rigid support such as a door cannot be found, an automobile robe or blanket, if available, may be used for conveyance of the victim, as follows. If a neck fracture is suspected and the victim lies face up, the blanket, rolled tightly lengthwise for about two thirds its width, is placed alongside him with the rolled portion next to his body. One assistant steadies the head in line with the body, as before, while one or two others tuck the blanket roll carefully under the victim and gradually unroll it beneath him, little by little, working slowly and smoothly, until the victim lies on the fully opened blanket. If the person with a neck injury lies face down, the head should be steadied, the arms brought above the head, and the body then rolled slowly over on to the blanket, which has been stretched out beside him. The arms may then be brought to the sides. In this maneuver, of course, care must be exercised to keep the head, trunk and extremities in line and not allow the neck to be twisted or bent.

If the victim has a broken back and lies face up, he may be rolled over onto the open blanket in the same way as described for a rigid support.

If, however, he lies face down, he may be lifted by two assistants, one grasping him beneath the arms and the other around the thighs just above the knees, and placed gently, still face down, on the open blanket.

Once on the blanket, he may be lifted and carried between two assistants, who firmly grip the blanket on each side of the victim at the level of

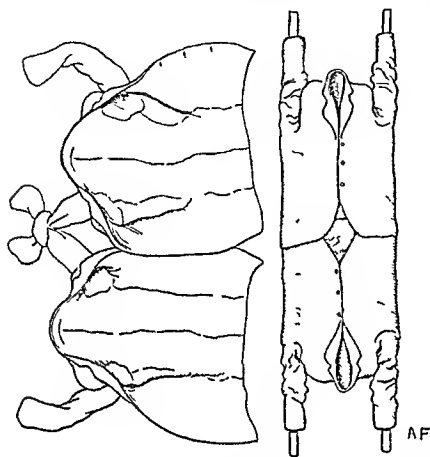


FIGURE 7 Two Methods of Improvising an Emergency Stretcher with Coats or Jackets

his shoulders and the middle of the thighs. In the event of neck fracture, head support must be maintained by a third assistant throughout transportation.

It happens sometimes that not even a robe or blanket can be found. Improvisation may still be possible. If two coats or jackets are stretched out

side by side, one is buttoned to the other, and the ends of the adjacent sleeves are tied together, a suitable blanketlike support will have been made (Fig 7). Better still, if two long poles or saplings can be found, a stretcher may be improvised with the two coats as follows. The open coats are stretched out on the ground, tail to tail. Each pole is slipped through the sleeve of one coat and the corresponding sleeve of the other, and each coat is buttoned. This provides a very serviceable stretcher by which two people, grasping the ends of the poles, can transport even a heavy person.

* * *

In conclusion, physicians who are teaching first-aid classes must always bear in mind the fact that the listeners are not actual or potential physicians. Thus, too much knowledge on the layman's part is not taken for granted, simple terms and language that they are sure to understand will be used, and the scope of instruction will be restricted to matters intimately concerned with first aid for fractures. About all, one should stress the points that, whenever possible, medical assistance should immediately be summoned and that the instruction given is for the sole purpose of protecting the victim from further injury until he can receive professional care.

The foregoing suggestions have been made in the hope of lightening to some extent the burden assumed by the physician who volunteers to instruct laymen in emergency splinting. The result of personal experience in this type of instruction, these methods have been tested and found practical and effective. They are not represented as necessarily the best, certainly not the only, procedures that may be followed. But, if adopted, they will be found simple to teach and reliable in application.

1001 Park Avenue

THE EFFECT OF POSTOPERATIVE INTERCOSTAL-NERVE
BLOCK ON PULMONARY VENTILATION*

ARNOLD STARR, M.D.,† AND SAMUEL GILMAN, M.D.‡

BOSTON

A SIGNIFICANT decrease of pulmonary ventilation following upper abdominal incisions has been repeatedly demonstrated.^{1,2} Figure 1A is a spirometric record obtained with a Collins metabolism apparatus on a forty-six-year-old woman breathing air. From this tracing, it may be

vertical right rectus-splitting incision: the tidal air measured 280 cc., the respiratory rate 22 per minute, the vital capacity 1400 cc., and the minute pulmonary volume 6160 cc. This represents a postoperative reduction in vital capacity of 20 per cent, and in minute pulmonary volume of 15 per

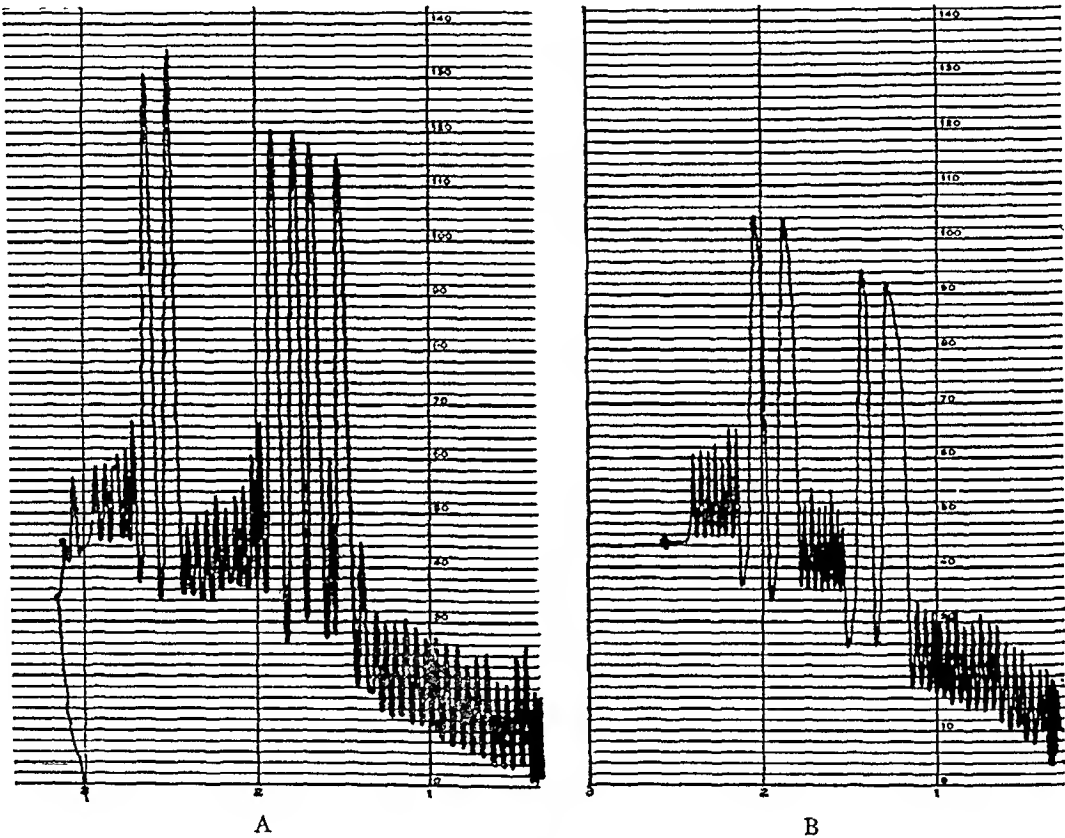


FIGURE 1. Spirometric Records before and after Choleldochostomy.

	A	B
Tidal air	400 cc.	280 cc.
Respiratory rate	18	22
Vital capacity	1800 cc.	1400 cc.
Minute pulmonary volume	7200 cc.	6160 cc.

calculated that the tidal air is 400 cc., the respiratory rate 18 per minute, the vital capacity 1800 cc. and the minute pulmonary volume 7200 cc. Figure 1B is a tracing from the same patient, taken in a like manner, twenty-four hours after choleldochostomy had been done through a

cent. A reduction in pulmonary ventilation is the usual change following upper abdominal incisions in women. Beecher² found an even greater reduction in vital capacity in men following upper abdominal operations. Reduced pulmonary ventilation has been ascribed to inhibition of respiratory excursion, to tight dressings, which restrict the costal margins, to splinting of the abdominal musculature resulting from pain in the wound, and to decreased diaphragmatic excursion caused by intestinal dis-

*From the Department of Surgery and the Department of Anesthesia, Beth Israel Hospital.
†Instructor in surgery, Tufts College Medical School; junior visiting surgeon, Beth Israel Hospital.
‡Assistant in anesthesia, Harvard Medical School; assistant in surgery, Tufts College Medical School; chief anesthetist, Beth Israel Hospital.

tion. Expansion of the lower lobes of the lungs follows closely the movements of the sixth, seventh, eighth, ninth and tenth ribs and their attached muscles. The diaphragm is the dominant organ in facilitating ventilation of the lower lobes, as Keith³ has shown. The lower sets of ribs are especially adapted to act with the diaphragm and are an intrinsic part of the diaphragmatic mechanism. Since the oblique abdominal muscles are antagonists to the diaphragm, the spasm induced in them by upper abdominal incision prevents full excursion of the diaphragm as well as of the lower ribs. These factors are involved in the interference with normal pul-

monary ventilation. Since this procedure could cause intercostal muscle paralysis in addition to relieving pain, the injection of sensory and motor branches to the upper abdomen only, according to Bartlett's⁹ technic, appears to be more logical.

This report deals with the effect on pulmonary ventilation of relief of the postoperative wound pain of upper abdominal incisions. Spirometric tracings were made twenty-four hours postoperatively before and after intercostal anesthesia. The Bartlett technic was used. The sixth to the tenth intercostal nerves of 8 patients who had had operations on the biliary tract were injected in the mid-

TABLE 1 *Effect of Unilateral Intercostal Nerve* Block on Pulmonary Ventilation*

Case No	RESPIRATORY RATE		TIDAL AIR		MINUTE PULMONARY VOLUME		VITAL CAPACITY		INCREASE IN VITAL CAPACITY
	BEFORE BLOCK per min	AFTER BLOCK per min	BEFORE BLOCK cc	AFTER BLOCK cc	BEFORE BLOCK cc	AFTER BLOCK cc	BEFORE BLOCK cc	AFTER BLOCK cc	
1	30	25	240	200	200	5000	880	1170	27
2	15	16	240	260	3600	4460	880	1080	23
3	24	21	480	520	11520	11440	1370	1520	12
4	25	25	280	280	000	7000	1040	1200	15
5	25	35	280	780	000	9800	580	780	31
6	30	30	280	280	8400	8400	480	690	25
7	23	25	280	320	6440	8800	520	680	31
8†	18	18	280	280	5080	5000	640	640	0
Average									23

*Nerves of sixth to tenth dorsal vertebrae

†Block partially effective ? gastric dilatation

monary ventilation and, presumably, are the basis for the occurrence of postoperative pulmonary complications, especially in the lower lobes.

Relief from pain in upper abdominal incisions, by relaxing the reflex spasm of the somatic musculature involved, should therefore improve pulmonary ventilation. Capelle⁴ relieved painful spasm in the wound by continuous novocain infusion and reported a resulting improved vital capacity and thoracic excursion. This procedure is impracticable because of the danger of toxicity from the continued administration of the anesthetic as well as interference with wound healing. Collins⁵ found an increase in vital capacity following infiltration of the wound with an aqueous solution of Eucupin and novocain. Zollinger⁶ injected an almond oil solution of Eucupin base, ethylaminobenzoate and benzyl alcohol into the intercostal nerves of 15 patients who had had upper abdominal operations. By comparing the resulting average vital capacity with the postoperative average determined previously by Cutler and Hoerr,⁷ he concluded that the decreased pain of upper abdominal incisions following intercostal-nerve block increased vital capacity. On the basis of 2 favorable cases, Gius⁸ recommended paravertebral novocain injection into the intercostal nerves for the improvement of respiratory function in patients

axillary line on the right side to desensitize the upper abdominal wall without affecting the intercostal muscles, whose nerve supply leaves the main intercostal trunk posterior to the midaxillary region.

The anesthetic solution used in this study was 0.2 per cent Eucupindihydrochloride and 1 per cent procaine hydrochloride in Ringer's solution. Although this solution had been used in patients by Collins, its possible damaging effect on various tissues and cavities was first tested by us in rabbits, and no harmful effect was observed. Following intercostal nerve block, anesthesia persisted for three or four hours, and analgesia remained for more than twenty-four hours, when abdominal pain returned, it was mild in every case. Longer acting agents, such as oily solutions of anesthetic substances, might be more desirable, but since Duncan¹⁰ observed serious degeneration in the motor nerves of the cat following the use of these anesthetic mixtures, they should be applied with caution.

Table 1 summarizes the data on pulmonary ventilation in a group of respiratory tracings obtained before and after intercostal nerve block twenty-four hours after an upper abdominal procedure. Following relief of upper abdominal wound pain by intercostal nerve block, the respiratory rate shows

no constant change; in 3 cases, the rate was decreased, in 2 it was increased, and in 3 it was not altered. The tidal air likewise showed no consistent change: in 1 case it was decreased, in 3 it was increased, and in 4 it was unchanged. The vital capacity showed a moderate increase in 7 of the 8 cases following relief of wound pain. In Case 8, the block was only partially effective, and there was some gastric dilatation, which may account for the lack of increase in vital capacity. The average increase of vital capacity in this group of cases was 23 per cent. The minute pulmonary volume showed no constant change, as one might expect, since the respiratory rate and tidal air were not altered in any constant direction.

Although the increase in vital capacity following relief of wound pain by intercostal-nerve block was of itself significant, other benefits were noted. The patients moved about more readily. Coughing was not only easier but also more effective. In 1 striking case, a patient who had high fever, rapid pulse and evidence of consolidation at the lung bases for forty-eight hours after epigastric herniorrhaphy obtained rapid relief of pulmonary signs and symptoms and became afebrile twelve hours after intercostal-nerve block, which effectively relieved the wound pain. This improvement was almost certainly due to the facts that cough became

easier and that the patient was able to raise a large quantity of thick sputum. Although relief might have occurred in spite of nerve block, the patient's immediate appreciation of increased comfort in breathing and in coughing was very definite.

CONCLUSION

The relief of upper-abdominal-wound pain by intercostal-nerve block improves the vital capacity and benefits the patient in other respects. The procedure is therefore worthy of more frequent application.

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MEDICAL PROGRESS

ARTERIAL HYPERTENSION*

ROBERT W. WILKINS, M.D.†

BOSTON

IN the last two years, a tremendous amount of work has been done in an attempt to solve the problems of arterial hypertension. Although much has been learned concerning the mechanisms of the renal types of hypertension produced experimentally in animals, and also of their clinical counterparts occurring naturally in man, little of practical value has been added to the methods of preventing or relieving the disease in human beings.

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*From the Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals, Boston, and the Department of Medicine, Boston University School of Medicine.

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†Associate professor of medicine, Boston University School of Medicine, and member, Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals.

HYPERTENSION OF RENAL ORIGIN

Animal Experiments

Pathologic physiology. It seems clear that the arterial hypertension produced in animals by interference with the blood supply of a kidney^{1, 2} is due to the increased pressor activity of the blood leaving that kidney (Fig. 1).³⁻⁶ Furthermore, it appears that this hypertension may be moderated by the presence of a normal kidney,^{7, 8} which can reduce the pressor properties of blood that has passed through the so-called "ischemic" kidney.⁶ Although the procedures used to produce this type of hypertension may be severe enough actually to reduce the blood flow through the kidney, they may be so nicely adjusted that they are exactly balanced by the ensuing responses in renal hemodynamics and systemic arterial pressure, and thus result in no significant change in renal blood flow.^{9, 10}

Strictly speaking, therefore, it may be inaccurate to apply the term, "renal ischemia," to the circulatory disturbance produced in the kidney. It has been shown that the reduction of arterial pulse pressure within the kidney is probably the abnormality that initiates and maintains the renal type of experimental hypertension.¹¹

The hypertension produced in animals by clamping of the aorta just above the renal arteries (simulating coarctation) seems to be of the renal

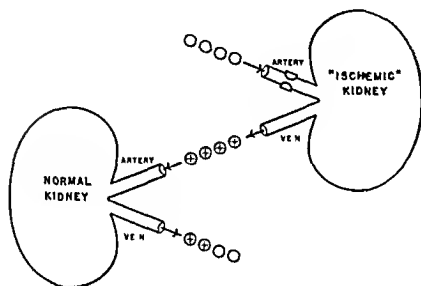


FIGURE 1 Diagram of the Probable Mechanism of Renal ('Ischemic') Hypertension

The blood (circles), on passing through the ischemic kidney (with a clamp on the artery), acquires increased pressor (+) activity but, after passing through a normal kidney, loses some of this activity

type.^{6 12 13} Intermittent occlusion of the renal artery, up to thirty minutes daily, does not cause a persistent elevation of arterial pressure,¹⁴ although there may be a brief rise of pressure immediately after the release of the occlusion.¹⁵⁻¹⁷

In animals with renal hypertension, more refined methods of measuring renal hemodynamics^{18 19} have revealed evidence of vasoconstriction of the efferent arterioles of the glomeruli (Fig 2).^{6 10 20}

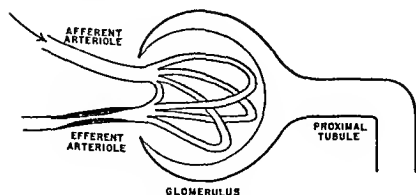


FIGURE 2 Diagram of a Glomerulus, Showing Constriction of Efferent Arteriole

This efferent arteriole constriction within the kidney itself is apparently part of the generalized vasoconstrictor response to the humoral pressor material elaborated by the ischemic kidney

Searches for the humoral pressor substance believed to be responsible for renal hypertension have proceeded in two directions: study of extracts of kidney, and study of hypertensive blood.

From the renal cortex, a protein extract may be obtained that, when injected intravenously into intact animals, produces hypertension similar to renal hypertension. Actually, this extract, renin,²¹ is not itself a pressor agent, but reacts with a pseudoglobulin fraction of blood (called "renin activator"²² or "hypertensin precursor"²³) to form a strongly pressor substance, called "angiotonin"²⁴ or "hypertensin,"²⁵ which, when injected intravenously, causes arterial hypertension and vasoconstriction generally,²⁶ including the efferent arterioles of the glomeruli.²⁷

Studies of the renal and peripheral venous blood of animals with renal hypertension have shown it to be more vasoconstrictor and vasopressor than normal.^{5 6 23 28 29} Treated chemically, such blood may yield material similar to renin, and to angiotonin or hypertensin. In addition, it may exhibit other properties differing from those of renin or angiotonin.^{6 30 31} However, the increased pressor activity of hypertensive blood has yet to be identified with the presence of one or more specific chemical compounds in abnormal amounts. That a whole series of such compounds is at least theoretically possible is indicated by the observations that similar substances are formed by the action of pepsin on renin activator (hypertensin precursor)^{32 33} and of anoxic kidney tissue (decarboxylating enzymes) on amino acids.³⁴

Treatment. It was shown early that experimental hypertension due to unilateral renal ischemia could be relieved by removal of the involved kidney.³ This fact settled a very important question, namely, whether hypertension is necessarily an irreversible state. The demonstration that renal hypertension, at least early in its course, is a functional disease, capable of relief, gave a hopeful outlook. This line of work has been extended, however, to demonstrate that, if a severe hypertension is allowed to persist, hypertensive vascular lesions may appear in widespread areas, including the presumably normal kidney.³⁵⁻³⁷ Furthermore, removal of the ischemic kidney at this stage may be followed not by complete relief but by a residual hypertension.^{36 38} Thus, it appears that a vicious circle may be established in which the hypertension due to impairment of renal circulation may produce lesions that cause further impairment and, as a result, more hypertension (Fig 3). The occurrence of malignant hypertension may be due to such a mechanism.³⁶

Since it was established that the normal kidney is able to decrease the pressor activity of renal hy-

pertensive blood, it was logical to search for a neutralizing or antipressor substance in the kidney. Renal extracts have been obtained that lower the arterial pressure of hypertensive but not of normal animals,³⁹⁻⁴¹ and decrease efferent arteriolar constriction.⁴² They also neutralize the effects of angiotonin.^{42, 43} Similar results have been obtained with tyrosinase⁴⁴ and amineoxidase,^{45, 46} which were used with the idea of destroying whole groups of pressor substances, if present. Unfortunately, these depressor materials have not yet been freed of toxic and pyrogenic properties, especially when given parenterally. Therefore, caution must be used in attributing their depressor action to the

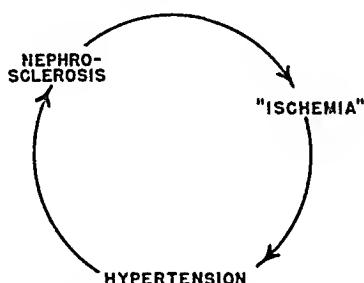


FIGURE 3. *Diagram of the Vicious Circle in Renal Hypertension.*

presence of specific neutralizing substances, since it has been shown that various nonspecific vasodilating or pyrogenic materials may have similar effects.^{47, 48}

Clinical Application in Human Beings

Parallel observations have been made in human beings confirming almost every important point learned about renal hypertension in experimental animals. Many cases of so-called "renal hypertension" in man have been reported,⁴⁹⁻⁵¹ including a number that have been relieved by removal of a unilaterally involved kidney.⁵⁰⁻⁵⁵ In children, such cases have been particularly dramatic.⁵⁶⁻⁵⁹

Studies of the renal hemodynamics in hypertensive patients have revealed evidence of efferent arteriolar constriction in the kidneys.^{48, 60} In those whose arterial pressure has been lowered following the removal of a diseased kidney, the efferent arteriolar constriction in the remaining kidney has been found to decrease.⁶¹ The total renal blood flow in unselected hypertensive patients is usually below normal.^{48, 60} However, differential function tests of the two kidneys in such patients have failed to reveal unilateral renal ischemia as a frequent finding in essential hypertension.⁶²

Clinical⁶³ and pathological^{53, 64} studies of cases of renal hypertension not relieved, or only partially relieved, by nephrectomy support the view that hypertension of some duration is accompanied by the development of hypertensive vascular

lesions, which may involve the normal kidney and thus produce a vicious circle (Fig. 3).^{36, 65} Structural changes have been found in the arterioles of muscles after renal hypertension of only a few months' duration.⁶⁶ Such lesions are indistinguishable from those found in essential hypertension.

Patients with coarctation of the aorta have been shown to have generalized diastolic hypertension,⁶⁷ and also efferent renal arteriolar constriction.⁶⁸ These observations are in accord with experimental studies suggesting that the arterial hypertension associated with coarctation is renal in origin.

The effects of renin,⁶⁹ angiotonin⁷⁰⁻⁷² and hypertensin⁷³ have been studied in human beings. Injected intravenously, these substances produce elevations of arterial pressure roughly proportional to the dosage used. The resultant hypertension is similar in many ways to clinical essential hypertension, but differs from it in certain respects, particularly in being accompanied by a considerable rise in venous pressure. Angiotonin produces efferent arteriolar constriction in normal human kidneys.^{20, 48, 72}

The use of depressor substances in the treatment of patients with hypertension has been restricted by the scarcity of the materials, and also by the toxic side reactions produced by certain preparations. In some patients, depressor renal extracts are said to lower the arterial pressure, decrease the efferent arteriolar constriction, and relieve the symptoms, especially headache and impairment of vision.^{30, 42} However, the effects are not consistent, and are complicated by the unpredictable variations of the disease, as well as by the occurrence of toxic reactions. Until standard preparations can be produced in adequate amounts for general trial, the value of such depressor substances cannot be finally determined.

NEUROGENIC HYPERTENSION

Hypertension of sympathetic nervous origin produced in animals by section of the moderator nerves^{74, 75} does not require the presence of the kidneys.⁷⁶ Hypertension due to increasing the intracranial pressure of animals apparently depends on reflex sympathetic stimulation of the heart, either directly through the cardiac nerves or indirectly through the mediation of the adrenal glands.⁷⁷

The role of the sympathetic nervous system in human hypertension remains obscure. Elevations of arterial pressure, especially in response to unpleasant stimuli, presumably occur in both normal and hypertensive persons through the mediation of the sympathetic nervous system. However, there is no direct relation between the amount of the

rise in arterial pressure and the degree of sympathetic vasoconstriction in the skin,⁷⁸ or in the muscular parts of the extremities⁷⁹ during such stimuli. Neither is there a loss of the pressor response after extensive splanchnic sympathectomy.⁸⁰⁻⁸¹ As yet, the sympathetic nervous mechanism in such responses is not clear. It appears that excessive responses (hyper-reactions) are commoner among hypertensive and prehypertensive patients than among persons who never develop hypertension.⁸² In fact, it seems that a tendency to abnormal elevations of arterial pressure is more important than the presence of renal disease in determining the subsequent development of sustained hypertension.⁸³ However, it should be noted that some hypertensive, hyper-reactive patients who have been relieved of their hypertension by the removal of an ischemic kidney have also been relieved of their hyper-reactivity.⁸⁴

A recent progress report⁸⁵ has summarized the knowledge to date concerning surgery of the autonomic nervous system in man. In some patients with essential hypertension, extensive sympathectomy definitely lowers the arterial pressure, especially with the patient in the upright position. It apparently does not increase the renal blood flow or decrease the efferent arteriolar constriction.⁸⁶⁻⁸⁸ Nor does it increase the blood flow in the calf.⁷⁹⁻⁸⁰ Sympathectomy, therefore, appears to be more a symptomatic than a specific form of therapy for hypertension. However, one may argue that lowering arterial pressure by any means impedes the development of hypertensive vascular lesions, especially in the kidneys, that might establish a vicious circle. Further long term studies⁸⁹ of the patients already operated on should eventually answer the question of whether sufficient, lasting beneficial results are obtained with surgical sympathectomy to warrant its use in arterial hypertension.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28301

PRESENTATION OF CASE

A fifteen-year-old schoolboy was admitted to the hospital because of headache and swelling and redness of the face of two days' duration.

For about four months prior to entry, the patient had frequent colds with considerable nasal discharge and postnasal drip. Four days before entry, the patient went swimming in a pool for the first time in several weeks. Two days later he developed a cold associated with severe right frontal headache. The next day the temperature ranged from 101 to 102°F. His headache persisted, and there was swelling of his right periorbital region to such an extent that he could not see out of the right eye. He had no chills, earache or sore throat.

The past and family histories were noncontributory. A year before entry, the patient had had an attack of frontal sinusitis.

On admission, the patient appeared acutely ill. The right eye was partially closed by swelling of the orbital tissues. There was tenderness over the right frontal sinus, with accompanying swelling and redness. Upward gaze was painful. Both frontal sinuses transilluminated poorly. Physical examination was otherwise negative.

The blood pressure was 140 systolic, 80 diastolic. The temperature was 99.4°F., the pulse 72, and the respirations 17.

Examination of the blood showed a white-cell count of 22,200 with 89 per cent polymorphonuclears, and a red-cell count of 4,690,000 with 15.3 gm. hemoglobin. The urine was normal.

Roentgenograms of the sinuses showed gross thickening of the mucous membrane of the right antrum, with polypoid changes; the sinuses were otherwise clear.

On the third hospital day, the temperature rose to 103°F. and the patient had a series of convulsive seizures in which the head and eyes turned toward the right and then generalized convulsive movements appeared, which were more marked in the right arm and leg than in those on the left. Between seizures, the patient was stuporous and showed right hemiparesis, with extensor plantar

response on the right, and marked stiffness of the neck. A lumbar puncture gave clear colorless fluid under an initial pressure of 230 mm. of water; the fluid contained 12 polymorphonuclears, 7 lymphocytes and 2 large mononuclears per cubic millimeter. The total protein was 58 mg. per 100 cc., the sugar 103 mg., the chlorides 690 mg., and the gold-sol curve 0012311000.

The seizures increased in frequency until they occurred about every five minutes. The patient was taken to the operating room, but because of severe respiratory difficulty, operation was deferred. The convulsions were controlled by ether anesthesia. Sulfapyridine and heparin were administered. The patient regained consciousness, but had right hemiplegia and aphasia. Two days later, the headache increased and the patient became less responsive. *Staphylococcus albus* was obtained from a blood culture taken on the second hospital day. On the sixth hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. FRANCIS C. GRANT*: We have here a child with obvious infection of the frontal sinuses, predominantly on the right side. On the third hospital day, a critical change in his condition developed, with an increase in temperature and convulsive seizures, which began with turning of the head and eyes to the right. These convulsive seizures were much more marked in the right arm and leg than in those on the left, whereas it was the right frontal sinus that was involved. He was stuporous and had a right hemiparesis and a Babinski sign on the right. The convulsive attacks were finally controlled, and the patient regained consciousness but had a right hemiplegia and aphasia. I presume that he was right handed.

DR. CHARLES S. KUBIK: Yes.

DR. GRANT: He must obviously have had a lesion of some type in the left cerebral hemisphere, with the possibility, of course, that, since this was an infectious process and since the sinuses were involved, there might have been multiple infectious processes.

I see nothing here about the eye grounds.

DR. KUBIK: They were normal.

DR. GRANT: I suppose he was too stuporous at any time to observe the visual fields.

DR. KUBIK: No; they were normal. He was not too stuporous for that at times.

DR. GRANT: There is nothing here about the conjunctiva of the right eye. Was that inflamed, and was there any ecchymosis?

DR. KUBIK: There was no ecchymosis, but quite a bit of edema.

*Professor of neurosurgery, University of Pennsylvania Medical School.

DR. GRANT: There was pain on upward movement of the eye, but apparently no difficulty in the movement of the eye.

DR. KUBIK: No; and no diplopia.

DR. GRANT: Are any x-ray films available?

DR. KUBIK: No; the x-ray films cannot be found.

DR. GRANT: Of course in a child of this age, one would not expect to find calcification of the pineal gland, but one might pick up calcification in the choroid plexus, and any change in its position might be of significance.

It seems to me that there are two possibilities. In the first place, we have the story that, four months prior to entry, the patient had frequent colds, nasal discharge and postnasal drip. Then he had this acute crisis, with infection of the sinuses, and *probably a blood-stream infection, because of the finding of Staphylococcus albus in the blood.* My suspicion is that the acute frontal sinusitis may not have been the important factor, but only a part of the picture that drove him into the hospital. He might conceivably have had a lesion resulting from the earlier infection, such as an abscess well forward in the left frontal area, that preceded the development of the right frontal sinusitis. The convulsive attacks are certainly suggestive of a left-sided lesion, although convulsive seizures are not a common occurrence in a subcortical abscess. It is quite conceivable that he had thrombosis of the longitudinal sinus. I imagine that this thought occurred to someone else, because the patient was given heparin during his hospital stay.

Am I allowed to elaborate on the way this case should have been handled, on the sixth hospital day, when an operation was performed?

DR. TRACY B. MALLORY: Yes.

DR. GRANT: Presuming that the patient's situation had improved and that the condition for which the heparin and sulfapyridine had been given had cleared up, I should have tapped the ventricles. If, as I suspect, the right ventricle was found to be larger than the left, I should have taken this as evidence of a lesion in the left frontal area and tapped there, expecting to find pus either on the surface or in the brain.

A PHYSICIAN: Is it likely that he had osteomyelitis?

DR. KUBIK: X-ray films taken with that in mind did not show an osteomyelitis.

A PHYSICIAN: Would you consider a subdural empyema?

DR. GRANT: I considered it, and I presume, if present, it would have been in the left temporal region, where it would possibly be picked up when one tapped for abscess.

DR. JAMES C. WHITE: Would you wait for the x-ray films to be positive before making a diagnosis of osteomyelitis?

DR. GRANT: No, I should not wait for them. I am presuming the physicians in charge nursed the patient for the respiratory difficulty he was in, and considered that if he ever was going to be operated on, he should be operated on then.

A PHYSICIAN: Do you think he had a right orbital abscess?

DR. GRANT: They did not do anything about it if he had. I take it that the orbital swelling disappeared. Did it disappear?

DR. KUBIK: No, it did not disappear; but it did not get any worse, and the patient was not operated on for orbital abscess.

A PHYSICIAN: Why do you lean to temporal-lobe abscess instead of frontal?

DR. GRANT: I am presuming that the boy had some difficulty with speech. They state that aphasia developed. I do not believe one can tell whether the effect of the lesion on the speech center was from in front or from behind or whether it lay directly in the speech center. I think we have to presume that the infection started in the sinuses in front. The lesion is more likely to be fronto-temporal than temporoparietal.

DR. WILDER PENFIELD: How can you tell irregularity of the ventricles?

DR. GRANT: You can find the difference in size between them by the amount of fluid withdrawn from each of them.

DR. PENFIELD: I wish I could.

A PHYSICIAN: Why do you object to putting air in?

DR. GRANT: I think this child was too sick. A ventricular estimation is sufficient.

A PHYSICIAN: Would you consider the injection of Thorotrast?

DR. GRANT: No, I think this boy was too sick. He had been carried through a respiratory collapse. The respiratory collapse is commoner with a cerebellar than with a frontal lesion. I do not have any data here regarding what immediately preceded the severe respiratory difficulty. Was there an accompanying drop in pulse, or was it purely respiratory? Was it due to positional change on the operating table or to the administration of anesthesia?

DR. KUBIK: It occurred before the anesthesia was started. He began to have seizures, almost constantly, and then stopped breathing. They telephoned from the operating room, as a matter of fact, that the patient had died.

A PHYSICIAN: Is there any relation between the trouble and the spinal puncture?

Dr. GRANT. I should presume that they would not remove any amount of fluid—just a drop or two to get the cell count.

A PHYSICIAN: They did the total protein and chloride.

Dr. GRANT: That requires about 8 cc I should not have done that. The record does not state what the sequence was. It may have been done some time before.

A PHYSICIAN: The convulsions were very frequent for an abscess, were they not?

Dr. GRANT: Yes; my conception about this boy is that he had a frontal abscess before the acute symptoms developed. Then sinus thrombosis produced cortical infection, irritation and convulsions.

A PHYSICIAN: Would you consider that the aphasia and hemiplegia were purely postconvulsive?

Dr. GRANT: No, because they came on, as I gather, late. I think you are correct in presuming they might have been. It simply says that the patient regained consciousness, then had aphasia and right hemiplegia.

A PHYSICIAN: What is wrong with the diagnosis of acute early encephalitis deep in the frontal lobe?

Dr. GRANT: The cell count was not particularly suggestive of encephalitis; it was not high enough, nor do I believe that the cells would have been predominantly polymorphonuclears. It looks more like abscess.

CLINICAL DIAGNOSIS

Subdural abscess, left motor area.

Dr. GRANT'S DIAGNOSES

Left frontal abscess.

Subcortical longitudinal sinus thrombosis, spreading to veins over left cortex and producing patchy meningitis and convulsive seizures

ANATOMICAL DIAGNOSES

Subdural empyema.

Thrombophlebitis of superior longitudinal sinus

Frontal sinusitis

Frontal osteomyelitis.

Dr. KUBIK: This patient was sent up to the operating room the first time with a diagnosis of subdural abscess, but because of the respiratory difficulty, the operation was postponed. The seizures were controlled with ether. He regained consciousness, but the hemiplegia and aphasia persisted. Three days later, he became worse, and a left subdural empyema was drained through a lateral frontal burr hole. The patient had a very stormy convalescence, with a number of convulsive seizures, but he finally pulled through and recovered

completely from the aphasia and hemiplegia. In the two years following his illness, he has had three or four seizures, and he is now taking dilantin. There was no x-ray evidence of osteomyelitis at the time of operation or for two or three weeks after that. Then we stopped taking x-ray films, and he was discharged after about seven weeks. Two weeks later, he came back with frontal osteomyelitis, demonstrated by x-ray study. This was operated on, and at the operation, the superior longitudinal sinus was found to be thrombosed. It seems likely that the thrombophlebitis preceded and was responsible for the subdural injection.

CASE 28302

PRESENTATION OF CASE

A fifty-five-year-old Canadian toolmaker was admitted to the hospital because of nausea, diplopia, vertigo, headache and spells of unconsciousness and disorientation occurring over a period of at least six weeks.

The patient had suffered from "migraine headaches" most of his life. These appeared about once a month and were accompanied by scotomas, nausea and vomiting. Four years before entry, the patient was in an automobile accident. He struck the left side of his head and was unconscious for a few minutes. Subsequently, there was insidious appearance of irritability, lack of judgment, memory loss and disorientation. These personality changes became progressively more marked. One year before entry, the usual headaches changed character, becoming occipital, with pounding radiation to both frontal regions and associated nausea, vomiting and vertigo. Eight months before entry cholecystectomy was performed at a community hospital; "stones" were found. Six weeks before entry, there was marked increase in the nausea and vomiting that accompanied the headaches. The patient went to a community hospital, where "an old duodenal ulcer" was demonstrated roentgenographically; treatment by the Sippy diet afforded no relief. After three weeks, the patient was transferred to another community hospital. The headaches continued as before, and the patient suddenly became comatose during the course of one. A lumbar puncture showed an initial spinal-fluid pressure equivalent to between 350 and 375 mm. of water. His pulse rose from 40 to 100 following the puncture, and there was temporary relief of symptoms. He was then transferred to this hospital.

On admission the patient was disoriented, vomiting and complaining of dizziness and double vision. There was evidence of recent weight loss and dehydration. The heart, lungs and abdomen

seemed normal. The neck was stiff, and there was a Kernig sign. The pupils were unequal, alternately enlarging and contracting. The optic disks were normal. There were questionable hypesthesia and hypalgesia in the left trigeminal-nerve field. The musculature of the trunk and extremities was generally wasted and flaccid, possibly more so on the left than on the right. The tendon reflexes were hypoactive and equal.

The blood pressure was 120 systolic, 80 diastolic. The temperature was 99°F., the pulse 44, and the respirations 15.

Examination of the blood showed a white-cell count of 16,700 with 71 per cent polymorphonuclears, and a red-cell count of 4,900,000 with 85 per cent hemoglobin. The urine showed a ++ test for albumin.

Roentgenograms of the skull showed no abnormalities. A roentgenogram of the chest showed only a few small areas of calcification in the right lung.

The patient became increasingly stuporous. On the second hospital day, bilateral occipital burr holes were made, under local anesthesia. Clear colorless fluid was obtained from both ventricles. The pressure was considerably increased, particularly on the left. The fluid from the left ventricle showed 34 polymorphonuclears and 12 lymphocytes per cubic millimeter with a total protein of 36 mg. per 100 cc. The fluid from the right ventricle showed 62 polymorphonuclears and 28 lymphocytes per cubic millimeter with a total protein of 44 mg. per 100 cc. The gold-sol curve was 0001210000, and the Wassermann reaction was negative.

Following the tap, the patient seemed improved. Adequate hydration was obtained by vigorous intravenous therapy. Ventricular tap was repeated on the second night in the hospital because of the return of drowsiness, disorientation and a slow pulse, with spasticity of the left arm and leg. Twelve cubic centimeters of orange fluid was aspirated, with improvement in the patient's condition. During the next few days, much restlessness necessitated paraldehyde sedation. A right hemiparesis appeared. An electroencephalogram suggested "electrical pathology" in the right frontal lobe. A ventriculogram performed on the third hospital day showed slight dilatation of the lateral ventricles, more marked on the left, and slight widening of the third ventricle; the surface filling showed some widening of the sulci. No tumor was demonstrable. On the eighth hospital day, bilateral temporal burr holes were made under local anesthesia, and the subdural space was explored without significant findings. Subsequent

lumbar punctures gave xanthochromic fluid, with an initial pressure of 440 mm.

The patient remained restless and unco-operative, constantly pulling off his dressings. Ultimately the left occipital burr hole became septic. On the twenty-third hospital day, the temperature rose to 104°F., and there was patchy bronchial breathing, with moist rales at the base. Sulfapyridine was given, but death occurred on the following day.

DIFFERENTIAL DIAGNOSIS

DR. JOST MICHELSEN: This is a very complex story, but one conclusion seems to be fairly safe: shortly before and on admission to the hospital, this patient had an intracranial lesion that produced an elevation of intracranial pressure. The findings on lumbar puncture in the outside hospital and on ventricular examination in this hospital bear out that point. Additional evidence can be derived from the facts that, following the lumbar puncture, the pulse rose from the very slow rate (40) to 100 beats per minute and that there was temporary relief of symptoms. In view of these findings and observations, the absence of papilledema is of little significance.

The questions arise, Where in the cranial cavity was this lesion localized, and what type of lesion did this patient have? Let us start with the findings on admission. The patient complained of double vision. We do not know which eye muscles or nerves were involved. Weakness of the sixth, as well as of the third, nerve can be interpreted as general signs of pressure. The pupils were unequal, and there was a hippus. Perhaps these signs, together with the rigidity of the neck and Kernig sign, suggest that there was a tentorial pressure cone, which produced compression of the midbrain. Hypesthesia and hypalgesia of the left trigeminal field may be caused by a lesion anywhere in the course of the trigeminal nerve from the gasserian ganglion to the pons. The flaccidity of all muscles and corresponding sluggishness of the tendon reflexes do not mean very much if we consider the poor general condition of the patient on admission. Later, spasticity of the left arm and leg developed, apparently without weakness. I wonder if the observer made a distinction between spasticity and rigidity. If the change of muscle tension involves both the flexor and extensor muscles, it should be called "rigidity," but if the antigravity muscles are chiefly involved, the condition should be designated by the term "spasticity." Rigidity is found clinically in diseases of the extrapyramidal system; spasticity arises from lesions of the pyramidal system below the level of the cortex or, if of the

cortex itself, from combined involvement of the motor area and the extrapyramidal area.

During the next few days, right hemiparesis appeared. This time the state of the involved muscles is not given. Nor is it mentioned whether the patient became aphasic. Was he right handed or left handed? The electroencephalogram indicated "pathology" in the right frontal lobe. X-ray films of the skull were normal, and hence the pineal gland was in the midline; and the ventriculogram failed to demonstrate a shift or filling defect of the ventricular system. Consequently, we must assume, contrary to the localization by the electroencephalogram, that the process was a diffuse one and certainly not limited to one hemisphere of the brain.

The question of the type of lesion is not less involved. A brain tumor can be ruled out. The absence of changes in the ventriculogram is not compatible with such widespread involvement by tumor. There is no evidence of a primary focus to indicate multiple metastases to the brain: the albumin in the urine is not sufficient evidence, and no other changes of the urinary tract are reported.

Thus, there remain to be considered subacute or chronic, vascular or inflammatory lesions. I say subacute or chronic lesions because it is difficult to determine from the history when this fatal disease started.

The patient had suffered from headaches most of his life. Their periodic occurrence and association with scotomas, nausea and vomiting are indeed suggestive of migraine, but it must be kept in mind that there are other conditions with constant organic pathology that give rise to similar perineuric manifestations first, and reveal their true character later. The commonest lesions of this type are hemangiomas of or near the occipital lobe. This possibility, however, is remote, because a hemangioma should have been shown in the ventriculogram.

The next point that must be settled is the possible relation of the head injury to the lesion that resulted in this man's death. Following the injury, he developed symptoms such as irritability, lack of judgment, memory loss and disorientation. The underlying pathology of such a postconcussional syndrome may be widespread physical damage to the brain, and I assume that the asymmetrical dilatation of the lateral ventricles and the widening of the third ventricle, as well as of the sulci, demonstrate objectively this pathology in the form of atrophy of the brain. But this alone did not account for the signs that the patient developed in the last stage of his disease. He may have had a subdural hematoma in addition to the other damage to his brain. This is a good possibility. The delayed onset of symptoms in subdural hematomas is not unusual, and the clinical picture is so varia-

ble that often the diagnosis cannot be made without trephine exploration. Such exploration was carried out on the eighth hospital day, without significant findings. It seems to me that it should have preceded the other operations. One can assume, however, that the patient did not have a subdural hematoma; furthermore, the ventricular puncture performed as the first procedure on the second hospital day yielded valuable information. There was an increase of cells and protein in the ventricular fluid. I am unable to evaluate the difference in pressure, cells and protein on the two sides, but the presence of white cells and the increase of protein in the ventricular fluid are very suggestive of an intracranial infection. Occasionally, brain tumor close to the ventricular system produces similar changes, but brain tumor has been ruled out.

It is unfortunate that the examination of the cerebrospinal fluid obtained in the outside hospital was incomplete, and it is equally unfortunate that the lumbar puncture was not repeated after his admission here, in spite of the beneficial results of the first lumbar tap. I should like to know about the cell count, the sugar, the chlorides and the findings on bacterial examination of the spinal fluid. The examination of the ventricular fluid apparently was also incomplete. The negative Wassermann reaction, however, eliminates a syphilitic infection.

Because of the lack of adequate information concerning the cerebrospinal fluid, the analysis from now on must be based more or less on guesswork. The trauma was not such as to suggest the development of an intracranial abscess or multiple abscesses. There was no evidence of an external compound fracture or cerebrospinal-fluid leak, and there was no other focus from which they could have originated. Did this man have an encephalitis? In reviewing the clinical findings once more, one wonders if rigidity of the neck and the Kernig as well as the other signs were not produced by the intracranial infection rather than by a pressure cone; in addition, signs of meningeal irritation are rare in encephalitis. Tuberculous meningitis may be considered. The negative chest plate does not rule it out. The temperature in tuberculous meningitis is often markedly irregular, which may explain the absence of any elevation in the beginning. A fungous infection of the central nervous system may be quite consistent with the course of the disease in this man. Metastatic carcinomatosis of the meninges is unlikely since, as previously mentioned, no primary focus was found. There is no evidence that the patient had a meningitis originating from the ears or sinuses, which apparently were normal. There was no osteomyelitis of the skull or any other source

from which an infection of the venous system of the brain may have originated. Furthermore, no definite relation can be established between the intracranial process and the abdominal lesions.

In summary, I should say that the patient suffered from migraine, gallstones and a duodenal ulcer. The head injury produced atrophy of the brain. In addition to these changes, the patient had widespread intracranial disease, with increased intracranial pressure and irritation or infection of the meninges. Brain tumor is ruled out. Single or multiple intracranial abscesses are considered unlikely. Metastatic involvement of the brain and meninges is eliminated. Tuberculous and Torula meningitides, as well as encephalitis and other forms of meningitis and thrombophlebitis, are unlikely. In other words, a definite differential diagnosis of the intracranial process in the final stage is impossible. There were terminal bronchopneumonia and wound sepsis.

CLINICAL DIAGNOSES

Encephalitis (type undetermined).
Cerebral atrophy.
Terminal bronchopneumonia.

DR. MICHELSEN'S DIAGNOSES

Migraine.
Gallstones.
Duodenal ulcer.
Widespread intracranial disease (meningitis? encephalitis?).
Terminal bronchopneumonia.
Wound sepsis.

ANATOMICAL DIAGNOSES

Carcinoma of stomach, with metastases to meninges, brain and left adrenal gland.
Operative wounds: bilateral burr holes, occipital and temporal; cholecystectomy; and appendectomy.
Subdural abscess, postoperative.
Lateral-sinus thrombosis, acute.
Congenital anomaly: extreme hypoplasia of left kidney, with ureter draining into seminal vesicle.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient puzzled the clinicians in charge of this case on the ward quite as much as it has Dr. Michelsen. They were never willing to commit themselves to a definite diagnosis. When the patient first came in there seemed to be a slight though remote chance of subdural hematoma, and the original burr holes were made primarily with the purpose of ruling out this one potentially remediable condition. When nothing was found, the impression shifted somewhat in favor of encephalitis, which was the final diagnosis on the death report.

At autopsy, obvious sepsis of the operative wound was found, which had extended through one of the burr holes to produce a localized subdural abscess. There was also a fresh, nonocclusive thrombosis of the lateral sinus. The meninges elsewhere over the cortex showed injection, and thickening and opacity of the arachnoid were also present. It was assumed that this represented a rather chronic meningitis. In the rest of the examination, numerous lesions were found that did not seem to have any connection with the cerebral process. There was a healed ulcer of the duodenum, and a second, still active, ulcer in the prepyloric area of the stomach. The gall bladder had been removed, and there was some dilatation of the common bile duct and hepatic duct. There were anomalies of the urinary tract. The left kidney could not be identified. The left ureter was completely atretic and emptied into the left seminal vesicle instead of entering the bladder at the trigone. The right kidney showed compensatory hypertrophy. A small tumor nodule was found in the medulla of the left adrenal gland. When the microscopic sections came through, it was at once apparent that the thickened arachnoid was diffusely infiltrated with tumor cells, some of which had a characteristic signet-ring appearance. Examination of the prepyloric ulcer showed its margins to be frankly carcinomatous, and the nodule in the adrenal gland also proved to be a metastasis. Although no gross metastases could be found within the cerebral substance, numerous minute foci of tumor cells were found on microscopic observation.

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SUBDURAL HEMATOMAS

THE formation and organization of a blood clot beneath the dura covering the brain, either completely composed of blood or partly mixed with cerebrospinal fluid, has long been recognized as a serious sequela of cerebral trauma, or as an occasional accompaniment of the blood dyscrasias and scurvy. A clear pathological concept of subdural hematomas, an understanding of how commonly the lesion may be found if constantly kept in mind by the clinician and an appreciation of the favorable influence of surgical treatment, when applied early, have been arrived at only in comparatively recent times. In 1933 and 1934, many erroneous ideas concerning subdural hematomas were erased from the record by Leary and his associates, and it is to

him that we are indebted for our modern concept of this disease. His work, as Munro points out in this issue of the *Journal*, is both "fundamental and unquestionably accurate." Thanks to Leary and subsequent investigators, these lesions can now be divided into two broad groups—the solid type and the mixed type, the latter in its common chronic stage often forming a fluid cyst, sometimes called a "hydroma" or "hygroma," a descriptive term of no particular significance.

Munro has shown that the solid type, usually thought of as the commonest of all subdural hematomas, is, in his experience as head of a large, active, neurosurgical service, the least common. The solid forms are of the nonexpanding type, some caused by trauma and others due to blood dyscrasias. They are often not diagnosed in their acute stage and only disclose themselves as fortuitous findings at autopsy in patients who, not infrequently, have become psychotic. It is this form of subdural hematoma that has received undue emphasis in textbooks and current medical thought, partly owing to the prominence given it by Putnam and Cushing in 1935. In Munro's series, it formed only 45 out of 310 verified cases. The lesions, however, are often favorably affected by surgical intervention, although the operative mortality may rise to 33 per cent, largely the result of deaths in the older age group.

The mixed forms are commoner than the solid types and are exclusively due to craniocerebral injuries. They consist of a mixture of blood and cerebrospinal fluid and expand during the course of their development. Their growth is often rapid in the first five weeks after injury and then somewhat slower for the subsequent two months. A subvariety, comprising the fluid group, accounts for many of the late manifestations of cerebral injury, including the debilitating post-traumatic neuroses.

The importance of both types lies in early recognition and surgical treatment. Theoretically, no acute subdural hematoma should ever reach the chronic stage. The diagnosis, possibly suspected from the clinical course of the patient, must usually

be confirmed by exploratory trephination, trans-temporal by preference and bilateral if necessary. Such an operation, in Munro's experience, is never contraindicated in "a patient who has been knocked unconscious by a blow on the head and who is not getting better or is getting worse under adequate lumbar-puncture and fluid therapy." If, as Munro rightfully concludes, these patients are not progressing favorably, "the responsibility rests with the physician to recognize the possibility that a mistake has been made in the diagnosis and that, as a result, he must investigate and treat the cause of this failure to recover by every means at his command." The "means" is the exploratory trephine, lightly, but not derisively, called "woodpecker surgery." In the hands of those specially skilled to carry it out, such surgical treatment not only prevents serious brain damage but also, in many cases, saves lives.

FIFTIETH ANNIVERSARY OF THE GRENFELL MISSION

ON August 4, 1892, a recent graduate of the London hospitals, Wilfred T. Grenfell, landed on the Labrador coast. On that bleak and isolated land, he found British fishermen and trappers who, amid great difficulties, earned a meager living for their families; there he also found poverty and disease unchecked and no physician on over hundreds of miles of coast. Fifty years ago, Grenfell saw and met the challenge, and for the rest of his life, he labored to improve the health and the lot of the fisherfolk of Labrador and northern Newfoundland. Last summer, the ashes of Sir Wilfred Grenfell were buried on the hill above the main mission hospital.

During the years of his active life, the Grenfell Mission, as it is known today, gradually took form, until its work covered over a thousand miles of coast. It grew to comprise five hospitals, as many nursing stations, three schools, a children's home, hospital ships, a marine railway and numerous industrial and agricultural facilities. In spite of his death, and under added difficulties engendered by the war, the work of the mission is

being carried on with these tools, under the supervision of a New Englander, Dr. Charles S. Curtis.

By the constant labors of the staff and through the education of the people, the years have witnessed many medical advances. Beriberi and other deficiency diseases, once all too common, have now nearly disappeared. Epidemics of typhoid fever and diphtheria, with their high mortalities, have been abolished by means of mass immunization. Tuberculosis, a very prevalent disease, is being brought under control. But perhaps most important of all, the people of Labrador now recognize the value of the aid extended to them and are willing to go to the nursing stations or hospitals during the early stages of their illnesses.

Today, as in the past,—when over sixty-five physicians from New England alone have given months or years of service,—much of the mission work depends on the continued support and enthusiasm of volunteer and paid workers. To these, Sir Wilfred Grenfell has left a legacy of spirit and courage for service.

MEDICAL EPONYM

POTT'S DISEASE

Caries of the spinal column and its effect were described by Percivall Pott (1713-1788), F.R.S., surgeon to St. Bartholomew's Hospital, in his "Remarks on that kind of Palsy of the Lower Limbs, which is frequently found to Accompany a Curvature of the Spine, and is supposed to be Caused by It: Together with its method of cure." This appears in Volume 3 (pages 349-385) of the edition of his works published in London in 1779.

The disease of which I mean to speak, is generally called a palsy, as it consists in a total or partial abolition of the power of using, and sometimes of even moving the lower limbs, in consequence, as is generally supposed, of a curvature of some part of the spine. . . . I have, in compliance with custom, called the disease a palsy; but it should be observed, that notwithstanding the lower limbs be rendered almost, or totally useless, yet there are some essential circumstances in which this affection differs from a common nervous palsy: the legs and thighs are, I have just said, rendered unfit for all the purposes of locomotion, and do also lose much of their natural sensibility, but notwithstanding this, they have neither the flabby feel, which a truly paralytic limb has, nor have they that seeming looseness at the joints, nor that total incapacity of resistance, which allows the latter to be twisted in almost all directions; on the contrary, the joints have frequently a considerable degree of stiff-

ness, particularly the ankles, by which stiffness the feet of children are generally pointed downward, and they are prevented from getting them flat upon the ground. . . I found, in infants, in young children, and in those who had been afflicted with the disorder but a small space of time, that the ligaments connecting the vertebrae, which formed the curve, were in some degree altered from a natural state.

When we attribute the whole of this mischief to the mere accidental curvature of the spine, in consequence of violence, we mistake an effect for a cause, and that previous both to the paralytic state of the legs, and to the alteration of the figure of the back bone there is a predisposing cause of both, consisting in a disordered state of the ligaments and bones, where the curve soon after makes its appearance.

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COMMITTEE ON MATERNAL WELFARE

CASE HISTORY SEPARATION OF THE PLACENTA,
COMPLICATED BY CHRONIC NEPHRITIS AND
HYPERTENSION, WITH DEATH OF THE
PATIENT, UNDELIVERED

A thirty-six-year-old multipara, approximately six and a half months pregnant, entered the hospital with acute abdominal pain. Her previous obstetric history revealed eight full term, normal children, the seventh pregnancy four years earlier having been complicated by toxemia and convulsions; this was followed by a normal pregnancy. There was no history of surgical operations or of scarlet fever, but she was known to have had chronic nephritis and hypertension for some years, and examination of the heart had, for some time, shown the hypertrophy consistent with this combination of diseases.

When she entered the hospital, the blood pressure was 230 systolic, 170 diastolic, there was a definite trace of albumin in the urine, and the sediment contained "casts." Examination of the eyes showed papilledema and signs of recent hemorrhage in the retina. The patient was kept under observation for forty-eight hours, at the end of that time, the acute abdominal pain recurred. Examination of the uterus showed it to be tender and firm. There was no mention of bleeding, but a diagnosis of separated placenta was made. Vaginal examination showed a multiparous cervix admitting two fingers. The patient was treated conservatively by the Dublin method: the cervix and vagina were tightly packed with gauze and a Spanish windlass was applied. Since the patient bled through this pack, a Voorhees bag was introduced into the cervix, the vagina repacked, and a transfusion given. She died undelivered, however, shortly after this.

Comment. From the medical standpoint, of course, this patient should never have been allowed

to become pregnant, and in the event of pregnancy, therapeutic abortion was certainly indicated. Any woman with chronic hypertension and nephritis jeopardizes her life when she undertakes pregnancy. This patient received no prenatal care whatsoever, and it is hardly fair to blame the medical profession for the catastrophe. Had she sought medical help earlier in pregnancy, therapeutic abortion should have been advised.

Separation of the placenta as early as the seventh month of pregnancy with complicating nephritis and hypertension is not common but, as evidenced here, quite possible. The blood pressure on entry, the albumin, sediment and casts in the urine, and the eye changes were evidence of very definite kidney damage. The patient was treated ideally—no criticism of her care is warranted. That she should, at this stage of pregnancy, bleed to the point of exsanguination when the cervix and vagina were packed is extremely unusual.

The treatment of this case should have begun with prophylaxis—by the avoidance of pregnancy or by therapeutic abortion and sterilization if pregnancy occurred.

MASSACHUSETTS MEDICAL SERVICE

INCOME LIMITS DETERMINED FOR SUBSCRIBERS

In an effort to create for the low income employee groups a larger measure of protection than a cash indemnity contract provides, the Massachusetts Medical Service faces the unwelcome necessity of determining income limits below which medical service contracts will be sold.

Medical service contracts refer, of course, to the services that will be provided by participating physicians for surgery, obstetrics and diagnostic x-ray studies. The term is used in contrast to the cash indemnity, or limited, contract that will be available to individuals in any income bracket above the specified limits. The Massachusetts doctors are initiating their program by offering this medical service contract only to members of employee groups whose individual income is \$2000 or less or whose family income is \$2500 or less. That such an arbitrary income limit is fair to both the physicians and the subscribers has been determined after serious study of medical service programs throughout the country.

The states of California, Oregon, Washington, Michigan, North Carolina and Pennsylvania, the counties surrounding Buffalo and Utica, New York, and the City of Dallas, Texas, have plans well under way. Within recent months, New Jersey and Colorado physicians have established statewide plans. In all these states, the highest level to which the medical service contract is available ranges from \$2000 to \$3000.

Decisions in these pioneer states were based on surveys of income levels, on the requirements of state insurance departments and on the need for a sufficiently broad base to render enough individuals eligible to meet the percentage requirements for group enrollment.

In California, physicians set the upper level of eligibility at \$3000, the base figure in a comprehensive health-insurance bill that was nearly passed. New Jersey established \$1600 as the level for the family, found it too low and raised it to \$2500 on the basis of government legislation proposed for the low-income group. Michigan established the limit at \$2000 for the individual and \$2500 for the family. Because the state insurance department would not accept lower levels, Buffalo set the limits at \$1800 for the individual, \$2500 for man and wife, and \$3000 for the family. Utica has no limit on eligibility.

BASIC FIGURES RESULT OF STUDY

In addition to the study of the plans operating in other states, the Massachusetts Medical Society has arrived at its \$2500 base figure through a study of income groups in Massachusetts. The most normal of recent years was the year 1939-1940, inasmuch as it was free from the abnormal influences of depression or boom. The study revealed that an individual income level of \$2000 accounted for 83.4 per cent of the wage earners and that a \$2500 family income embraced 91.4 per cent. In the present period of increasing wages, these percentages may be modified. With the increased cost of living, however, individuals within these fixed limits are even more in need of a medical-service program.

Employees whose individual or family incomes place them above the medical-service contract may be enrolled with their group on a cash-indemnity basis. They will receive cash payments for medical services in the amounts specified in their contracts. Since this cash-indemnity subscriber may then be charged by the physician the difference between the latter's fee and the amount guaranteed by the contract, there is virtually no alteration in the present financial arrangement between the private patient and his physician, except that the doctor is assured more prompt payment and the subscriber is enabled to pay his bill more easily.

Summarizing, then, the physicians of the state through the Massachusetts Medical Service are offering medical-service contracts, which comprise surgery, obstetrics and diagnostic x-ray services, to groups of employees whose individual incomes are \$2000 or less and whose family incomes are \$2500 or less, and cash-indemnity contracts for employees whose incomes are above these figures.

WAR ACTIVITIES

PROCUREMENT AND ASSIGNMENT SERVICE

DUTIES OF THE VARIOUS UNITS

The following memorandum concerning the duties of the various units of the Procurement and Assignment Service was recently issued by the executive officer, Major Sam F. Seeley, by order of the Directing Board:

Directing Board

1. Establishment of policies and procedures for the Procurement and Assignment Service.
2. Maintenance of liaison with the appropriate governmental officials and agencies and with the various professional groups.

Central Office

1. Maintain contacts with federal agencies relative to their needs for physicians, dentists and veterinarians, and consultations with these agencies regarding the possibilities of revision of their requests in consideration of the limited supply of professional men in these fields.
2. Prepare quotas of the minimum medical, dental and veterinarian services which should be retained for the civilian population, including private practice, hospital service, industrial service, public-health service and medical education.
3. Prepare quotas for allocating to the states the requests for physicians, dentists and veterinarians needed for war service (these quotas to be determined on the basis of the physician-population ratio in the state, the number of physicians already in service from that state and so forth).
4. Maintain rosters of physicians, dentists and veterinarians:
 - a. Total in the United States.
 - b. Those who have registered with the Procurement and Assignment Service.
 - c. These rosters to contain physician's age, qualifications, location and so forth.
 - d. From these rosters, which will be maintained by the National Roster, names of physicians, dentists and veterinarians with certain qualifications will be obtained from time to time.
5. Secure information for the various governmental agencies in regard to physicians, dentists and veterinarians, as to:
 - a. Availability for service other than in their present location.
 - b. Their professional and other qualifications.
 - c. Their willingness to serve in various capacities during the war emergency.
6. On the basis of this information, select the names of those physicians who meet the specifications of the requisitioning agency.
7. Co-operate with the various governmental agencies in obtaining the applications of those physicians thus selected for service.

Chicago Office

1. Maintain and keep up to date the confidential information concerning all physicians, dentists and veterinarians, with respect to character, type of practice, infringements of law and so forth, which must be considered by the Army, Navy and so forth in deciding whether individuals are qualified for commission.

2 Maintain confidential lists of the relative standing of all specialists (These lists have been developed through the facilities of the American Medical Association, the American Specialty Boards, the National Research Council and confidential advisers representative of the various specialties. This material is to be used by the requisitioning agencies as a basis for assignment of those now on duty and those who are candidates for commission)

3 Furnish assistance of a consultative and advisory nature to the Directing Board and to the various committees of the Procurement and Assignment Service (This includes the utilization of statistical data collected over a period of many years by the medical dental and veterinary medical associations)

Corps Area Committees

1 Supervise the work of the state committees in order that they will be reasonably uniform in the manner in which they carry out the policies of the Directing Board (This will require meetings of the corps area committees with state chairmen and visits by the corps area chairman to the states within his corps area)

2 Act as an appeal board in cases in which the individual physician, dentist or veterinarian, his community or his employing agency differs with the classification given by the state committee

State Committees

1 Obtain the overall enrollment of the professions in the state (This will require the maintenance of rosters in the state offices of those who have enrolled with the Procurement and Assignment Service and those who have not. The former lists will be obtained from the Central Office)

2 Survey local needs for professional services in conformity with the policies laid down by the Directing Board, and on the basis of these surveys determine how many physicians, dentists or veterinarians are needed in the various communities of the states to care for the civilian needs and how many can be released for service elsewhere

3 Determine which particular individual physicians, dentists or veterinarians can be considered available for service elsewhere (In view of the changing circumstances this will require constant reappraisal and obviously can be done only locally)

4 Pass on the availability, character and professional qualifications of individual physicians who are being considered for appointment for service elsewhere for example, for commissions in the Army, Navy and so forth, and

5 Co-operate with the state offices of the Selective Service System in determining whether physicians, dentists and veterinarians who are subject to classification by the Selective Service System are essential in their local communities

6 Maintain lists to be transmitted from the Central Office of those who have expressed their preference for service in industrial practice, civil practice in other communities, state and local health departments and institutions, and act as liaison between these individuals and the industrial organizations, civil practitioners and health departments and institutions desiring the services of these individuals in a temporary capacity for the duration of the war

7 Keep the Directing Board informed of conditions in the state, and bring to its attention matters which may involve general policies

8 Make periodical (weekly) reports to the Central Office of the names and addresses of those commissioned from the state, with information as to which of these have been serving as interns or residents

District or County Committees

1 Provide information, assistance and advice to the state committees in carrying out their functions (Local committees have no authority to make final decisions whether positions or individuals are essential or nonessential)

MISCELLANY

TUBERCULOSIS IN INDUSTRY

As mills and factories hum and as thousands of men and women swell the ranks of labor under the pressure of war industry, problems concerning the health of workers are in danger of being pushed aside. Tuberculosis is one of the notorious wasters of manpower. Special attention must be given to this disease, which affects and is affected by occupation. To help clarify concepts, a symposium on tuberculosis in industry (A symposium on tuberculosis in industry held at the Stranac Laboratory, Stranac Lake, N. Y., in June, 1941, a resume, *J A M A* 118 642-644, 1942 *Tuberculosis in Industry* 374 pp. New York: National Tuberculosis Association, 1942) was held at the Stranac Laboratory, where leaders in health and industry discussed problems that will also interest the general practitioner. A resume of the symposium follows.

The prevalence of tuberculosis in any community is determined by the general standard of living and by the number of open carriers. In particular occupations, the factors of selective employment and unfavorable environment modify the picture. If such factors work involving silence for example are dominant, the incidence in the wage earners will be different from that of their families.

The source of the great bulk of infections is a human carrier with a pulmonary cavity. Although the home is probably the place of most childhood and some adult contacts, many primary infections and more reinfections must occur in the place of work. Nurses, physicians and attendants on the sick encounter a real occupational hazard from infection itself; this hazard should be accepted as incidental to the professional life and hospital management should assume the obligation of minimizing opportunities for mass infection.

About 65 per cent more young women than men die of tuberculosis between the ages of fifteen and twenty-five. From a practical standpoint the employer of large numbers of women needs an effective medical department if he would avoid a tuberculosis problem. Race is a factor to be considered but it is so intricately associated with the effects of living standards and environment that its effects cannot be weighed. Nutrition is another important factor but also one of the most difficult to evaluate. The influence of fatigue has been studied in the automobile industry and in a steel mill, in neither of which there was evidence that this factor was responsible for any excess of tuberculosis. The belief that abnormal degrees of temperature and humidity lower resistance has little support. Trauma does not initiate a primary infection of the lungs.

Tuberculosis has been regarded as the great enemy of the printer (printers and printers have about 16 per cent more tuberculosis than all other occupied men), and in turn was attributed to lead poisoning which printers might have contracted. Certain studies indicate that neither lead absorption nor lead intoxication is the cause

Fumes and gases are inhalable, and many of them are sufficiently irritating to provoke severe inflammatory reactions. Mature judgment on the effects of gas used by the armies during the last war reversed the early opinion that this agent was responsible for the many cases of tuberculosis that developed. Routine annual examination of a large group of employees engaged in the manufacture of chlorine, phosgene, hydrofluoric acid and other irritating gases supports the view that exposure to irritant gases is not responsible for excessive tuberculosis.

The general thesis that inflammation of the lungs is necessarily unfavorable to the course of associated tuberculosis has little support. It is probably true that certain kinds of inflammatory reactions may have some influence. The increased incidence of tuberculosis that followed epidemic influenza may have been due in part to pneumonic complications.

In grain handlers exposed to high concentrations of organic dust in unloading lake steamers, 2.5 per cent of a group of 234 showed x-ray evidence of clinically significant tuberculosis, and another 2.3 per cent had old healed lesions. Socioeconomic factors, rather than grain dust, were thought to be responsible. Tobacco dust has been under suspicion as a cause of tuberculosis since Ramazzini's studies in 1700. Yet, in a modern cigar factory with a well-organized medical service and air-conditioned rooms, there was less tuberculosis than in the city where the plant was located. Metropolitan mortality figures for 1937-39 show an index for tuberculosis of 107 in cigar and tobacco factory operatives, but it should be noted that 75 per cent of the labor, which now produces only 25 per cent of the product, still works in small shops without health supervision.

Low rates for tuberculosis were found in the Saranac Laboratory studies of the cement and gypsum industries. The usual number of healed lesions was disclosed, so that opportunities for infections had not been lacking.

All these observations support the view that exposure to organic and nonsiliceous dusts has little influence on susceptibility to tuberculosis. Reports on foundries, quartz mining and the granite industry brought out that higher tuberculosis rates prevail in these trades, that there is a greater tendency for such infection to develop after the age of forty rather than earlier, and that the infection is extremely chronic, often giving no symptoms of intoxication or a positive sputum until shortly before death. In miners, the incidence becomes higher and the prognosis of associated tuberculosis worse as the silicotic reaction increases. Miners exposed to silica dust with no roentgenographic evidence of reaction showed little more tuberculosis than the other members of the community in which they lived. Foundries seem to be responsible for the least amount of tuberculosis, whereas the granite industry probably causes the most.

Vermont marble workers had two and a half times as much tuberculosis as the general population of the state (largely rural) exclusive of the granite center in Barre. By contrast, the rate for granite workers was one hundred and thirty times the general one.

The value of a good industrial hygiene program was brought out by the experience of the Eastman Kodak plant. This program costs \$10,500 annually, but it also costs \$3218 to treat one minimal case of tuberculosis. The attack rate in this plant has fallen from 2.3 at the outset of a study to 0.2 at the present time.

The complexities of compensation insurance carriers were discussed. One plan proposed was that evidence of tuberculosis in any form should preclude employment

in industries with silica or other proved hazards and that compensation should be allowed for all tuberculosis subsequently developing in such employment. In other industries, with no specific hazards, persons with healed tuberculosis should be permitted to work, but no compensation should be allowed for infections that might become active or develop during employment. In view of the evidence that old tuberculosis so rarely breaks down in any industry except industries with silica hazards, this appears most equitable.

In the summary, it was pointed out that, aside from nutrition and socioeconomic factors, silica is the only one that has a recognized effect on susceptibility to tuberculosis. Many industrial conditions popularly accepted as predisposing to this disease are without measurable effect. — Reprinted from *Tuberculosis Abstracts*, July, 1942.

NOTE

At a recent meeting of the College of Physicians of Philadelphia, the Alvarenga Prize was awarded to Dr. Edwin J. Cohn, professor of physiological chemistry at the Harvard Medical School, in recognition of his distinguished contributions to the knowledge of blood proteins.

CORRESPONDENCE

COARCTATION OF AORTA

To the Editor: In the December 27, 1934, issue of the *Journal*, I reported two cases of coarctation of the aorta, in father and son. In the former, the clinical diagnosis has been verified.

A. D. did heavy manual labor from the beginning of 1933 until he died on August 16, 1941. He took 1½ gr. of digitalis daily most of the time from 1934 until his death. Extrasystoles were present at each examination. These persisted when he omitted the digitalis. On April 17, 1936, his blood pressure was 192/102; on August 3, 1940, it was 210/106; and on May 10, 1941, it was 176/96. On the last date, he suffered from loss of memory, and moist rales were heard at the bases of the lungs; no paralyses and no abnormal reflexes were found. He was advised to rest and to continue taking digitalis. However, on May 18, he was found shingling a roof. At that time, the blood pressure was 182/94, and the lung bases were clear. In the late afternoon of August 16, the patient's car, which he was driving, collided with another automobile. He turned to his wife and asked how she felt. On being reassured that she was all right, he stepped from the car to the pavement and at once fell down. A physician who arrived shortly thereafter pronounced him dead.

At the request of an insurance company, the patient's body was exhumed, and an autopsy was performed by Dr. Benjamin Castleman on October 9. Just below the attachment of the closed ductus arteriosus, the lumen of the aorta was completely blocked. There were hypertrophy of the left ventricle and marked sclerosis of the coronary arteries. The aortic cusps were normal. The internal mammary arteries were four times the usual size. The abdominal aorta and the iliac arteries were small.

Immediately after the accident, and at the post-mortem examination, there was no evidence of severe traumatic injury.

W. G. WALKER, M.D.

11 Arlington Street
Brockton, Massachusetts

(Notices on page x)

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CESAREAN SECTION IN MASSACHUSETTS IN 1940*

ROBERT L. DENORMANDIE, M.D.

BOSTON

THIS report is the fourth of the five-year study of cesarean sections sponsored by the Massachusetts Department of Public Health and the Section of Obstetrics and Gynecology of the Massachusetts Medical Society.

Questionnaires were sent to one hundred and seventy-two licensed maternity hospitals, and replies were received from all except one small proprietary hospital. The care given the preparation of the replies varied greatly. The co-operation of those hospitals that replied carefully and intelligently to the questionnaires is appreciated. In thirty-nine hospitals, no cesarean sections were performed.

* * *

In Massachusetts in 1940, there were 66,496 live births and 1765 stillbirths, a total of 68,261. Of these, 56,935 were reported to us as having occurred in hospitals. Two thousand three hundred and twelve cesarean sections are recorded. One emergency section was done in a home. There were 21 hysterectomies, making a total of 2333 abdominal deliveries.

The incidence in 1937 was 1:30.3, in 1938, 1:28.7, in 1939, 1:32.2, and in 1940, 1:29.2.

Table I gives a summary of the abdominal deliveries. There was a greater proportion of elective sections than before, and a little larger percentage of low sections.

There were 26 of the extraperitoneal type, 16 being of the Waters type. All but 2 of the patients in this group lived. Twenty-two babies lived, but 5 were stillborn. The deaths are discussed below. It should be remarked that the convalescences in this group were greatly improved over those occurring in 1939. In 1 case of the peritoneal-exclusion type, the patient had a stormy convalescence because of sepsis, but eventually recovered. Two others developed sepsis, with stormy convalescence,

and made slow but final recovery. One patient was infected with gas bacillus but eventually recovered.

There were 34 Porro operations, or hysterectomy following immediately or shortly after the cesarean section. The indications for these 34 cases are

TABLE I. Summary of Abdominal Deliveries.

OPERATION	No. OF CASES
Cesarean section	2312
Emergency	1051
Elective	1247
Not reported	14
Type of operation	
Low	1235
Classical	992
Latzko, Waters or extraperitoneal	26
Porro	34
Not reported	25
In labor	757
Not in labor	1491
Not reported	64
Membranes ruptured	368
Membranes unruptured	1884
Not reported	60
Hysterectomy	21
Total	2333

varied. Eight were done for uncontrollable hemorrhage. One of these patients, a case of placenta previa, when operated on, was found to have a placenta accreta. Seven operations were done for fibroids of the uterus. In 5 cases, the only reason given was that the patient had had a previous section, but in only 1 of these had two sections been done. In 5 cases, a ruptured uterus was found. The following indications each accounted for 1 case: eclampsia, toxemia, pyelonephritis, age of patient (forty-four), a long labor and patient infected, and a shoulder presentation with a contraction ring. In 1 case, I have classified the indication as bizarre, — "necessity for pelvic operation." In 1 case, there was no recorded indication, and in the final case, the indication given in the questionnaire was "attempted breech extraction, with inability to deliver the head." That indication suggested very bad obstetric judgment, and on fur-

*Presented in part, before the Boston Obstetrical Society, January 20, 1942.

ther inquiry it was learned that the patient was in labor a long time and that x-ray examination showed a breech presentation with a definite hydrocephalic head. Since the fetal heart was heard, the operator did a section and then a Porro. In this group, 14 babies died, and 21 survived. Five of the mothers died, but these are reported under the maternal deaths.

Table 2 records the indications for the hysterotomies, and needs no comment.

Table 3 shows the various types of anesthesia used. The only change noted is the great increase in the use of spinal anesthesia. It should be mentioned that in 1 case the patient was prepared for

TABLE 2. *Indications for Hysterotomy.*

INDICATION	NO OF CASES
Cardiac disease	5
Hypertension	5
Pylonephritis	3
Tuberculosis	2
Separated symphysis	2
Manic depressive insanity	2
Chronic nephritis	1
Progressive muscular atrophy	1
Total	21

a section, was given a spinal anesthesia and died as the abdominal incision was made. The case cannot be classified as a death from cesarean section, but it is recorded among the maternal deaths

TABLE 3. *Types of Anesthesia.*

ANESTHETIC	NO OF CASES
Nitrous oxide, oxygen and ether	1355
Ether	261
Cyclopropane	144
Spinal	396
Nitrous oxide and oxygen	5
Avertin, and nitrous oxide, oxygen and ether	27
Local	32
Other	70
Not reported	22
Total	2312

occurring in Massachusetts in 1940. In the group classified as "other," there were various combinations of basic drugs with either cyclopropane, ether or nitrous oxide.

Table 4 presents the indications for operation in cases in which the baby was lost. As one might expect, emergency operations accounted for the large majority of these infant deaths. In the elective-section column, several can at once be excluded from criticism. In 2, the babies were macerated. Two mothers had diabetes. One had chronic nephritis, and the section was done in the interests of the mother. Three babies had malformations incompatible with life—meningocele, diaphragmatic hernia and congenital abnormality of the bile ducts. Five deaths in the elective column were assigned to monstrosities; all the fetuses

were hydrocephalic. Not all these cases had x-ray study before operation. Subtracting these 13 cases, there were still 52 elective sections in which the baby was lost. It is unnecessary to review these deaths. It is sufficient to call attention to the fact that serious criticism is justified when a baby is lost following an elective section. Either the time chosen or the technic is at fault, and the operators should rightly be reprimanded.

In the emergency column, as has been remarked in previous reports, it is doubtful if sections should

TABLE 4. *Indications for Operation in Cases with Death of the Baby.*

INDICATION	EMERGENCY CESAREAN SECTION	ELECTIVE CESAREAN SECTION
Separated placenta	49	0
Placenta previa	49	7
Toxemia	4	10
Eclampsia	3	0
Previous cesarean section	18	22
Inefficient labor	4	0
Disproportion	1	4
Contracted pelvis	3	5
Dystocia	2	0
Ruptured uterus	4	0
Previous operative attempts	2	0
Test of labor	4	0
Cardiac disease	1	2
Malposition	6	0
Monstrosity	6	5
Elderly primipara	1	0
Breech presentation	3	0
Previous surgery	1	3
Medical indications	0	4
Cervical dystocia	2	0
Previous disaster	0	1
Young primipara	0	1
Fetal distress	1	0
Uterine inertia	1	0
Prolapsed cord	1	0
Bicornate uterus	1	0
Bizarre	1	1
Not reported	1	0
Totals	169	65

have been done for the first two indications—separated placenta and placenta previa.

To go over each indication would make a tiresome review, but certain points should be noted. Under "monstrosity," there were 6 cases of hydrocephalus. The majority were not so diagnosed before operation. Malposition of the heart, congenital atresia of the esophagus, and diaphragmatic or ventral hernia cannot be diagnosed before operation, but major skeletal deformities should be, if careful x-ray films are taken.

The chief reason for the loss of the babies under the indication, "previous section," was prematurity. Either labor had begun or the membranes had ruptured before term. Many of these patients were operated on after they were in labor.

It is obvious that the number of babies lost is too large. The operators should weigh the probability of obtaining a living baby more carefully than they obviously did. It is surely questionable obstetrics to do an emergency section because a fetus shows distress, and then obtain a hydro-

cephalic baby. This is true of other indications. Until the infant mortality is reduced, the results in cesarean section cannot be regarded as satisfactory.

Table 5 shows the indications given for operation. It is to be expected that the operations for "previous section" will increase steadily because of the great number of new sections done each year.

I shall not discuss each indication, but there are certain comments that I wish to make. Many of

cause of a multiparous breech is not good obstetrics. Whether many of the transverse presentations could have had external versions or simple internal podalic versions at an elected time is a difficult question to settle, but there has been a great increase in the number of sections for this indication.

Under "dystocia," an attempt has obviously been made to use the test of labor in a greater number of cases. But the test of labor is a very indefinite

TABLE 5 *Indications for Cesarean Section*

INDICATION	NO. OF CASES	INDICATION	NO. OF CASES
Previous section	37	Associated medical conditions	51
Contracted pelvis and disproportion	350	Cardiac disease	27
Contracted pelvis	204	Tuberculosis	3
Disproportion	146	Diabetes	13
Placenta previa	211	Carcinoma of cervix	1
Separated placenta	109	Purpura hemorrhagica	1
Toxemia	10	Myxomatous gravid	1
Eclampsia	15	Fibrous cysts	1
Malposition of baby	113	Acute back	1
Breech	73	Chronic nephritis	1
Transverse	20	Paroxysmal tachycardia	1
Brow	4	Schizophrenia	1
Face	6	Early rupture of membranes	2
Compound	1	Previous obstetric disaster	73
Shoulder	2	Elderly primipara	57
Right occiput posterior	4	Young primipara	1
Cl in posterior	1	Obstructing tumors (fibroids)	21
Left parietal	1	Fetal distress	7
Type not noted	1	Prolapsed cord	4
Dystocia	29	Previous operative attempts	8
Dystocia	37	1st request or for sterilization	9
Labor without progress	31	Request	4
Test of labor	127	Sterilization	5
Cervical dystocia	44	Ruptured uterus	4
Contraction ring	3	Spontaneous	2
Uterine inertia	22	Previous section	2
Previous surgical operations	56	Bicornate uterus	1
Repair of perineum	21	Postmaturity	8
Amputation of cervix	16	Malformation of fetus	9
Myomectomy	5	Malformation of vagina	2
Pelvic surgery	3	Twins	3
Uterine surgery	3	Flotting head	3
Fracture of both bones lower leg	1	Varicose veins	1
Congenital hip	1	Bizarre	19
Previous abdominal operation	1	Not reported	63
Perineal abscess	1		
Acute appendicitis	1	Total	2312
Strangulated umbilical hernia	1		
Previous nephrectomy	1		
Previous operation on spine	1		

the sections for placenta previa were done at five, six or seven months' gestation, with no probability that the babies would live. The same thing is true of the indication, "separated placenta."

The number of cases done because of eclampsia in 1940 was larger than that in any previous year—15. Of course, when eclampsia occurs, somebody has erred, either the patient or the physician. But to subject a woman already desperately sick from eclampsia to a section is regarded by the majority of obstetricians as a doubtful procedure. In 1940, 3 eclamptic mothers died.

Under the indication, "malposition of the baby," an increasing number of sections are done for breech. A section on a primiparous breech may be justifiable in many cases. But to operate be

thing, varying from one or two hours to twenty-four or forty-eight hours, with or without rupture of the membranes. In many of the cases of "labor without progress," it was definitely stated that the patient had had only an occasional pain. In some cases of "cervical dystocia," the patient was not even in labor, and yet a section was done for that indication.

It is doubtful if everyone would agree on the indications classified under "previous surgical operations." Undoubtedly, many of these were justifiable, and to state dogmatically that they were not would be unfair. I have continually questioned the advisability of doing sections on so many patients who have had a repair of the perineum.

ating the indications, "pelvic and uterine surgery." Surely "fracture of both bones, lower leg" is specious. I cannot understand the indications, "perineal abscess" and "acute appendicitis." If the latter was a definite acute appendix, surely to follow it by a section was a very dangerous procedure. In this case, to quote the operator, "it was explained to the husband that a cesarean section was advisable since there would be a great danger of evisceration of the abdominal wound during normal labor, which was due in ten days."

The indications listed under "associated medical conditions" need little comment. It must be remembered that a section in a severe cardiac condition is a serious procedure and not always the best way to deal with the condition. Each year, deaths are recorded in this group, and in 1940 there were 3.

In previous reports, the reason for the increasing number of sections on diabetic patients has been mentioned. In 1940, there were 13 new sections for this condition, and 5 others were classified under "repeat sections." No mothers were lost, but 3 babies died, 1 was macerated, and 1 had a cystic kidney.

A somewhat astonishing indication is "acute back."

Following "associated medical conditions" in this table, one finds a miscellaneous list of indications. Some of these are valid, but others are not.

"Previous obstetric disaster" is in many cases a reasonable indication. But the circumstances surrounding the previous delivery must be thoroughly studied—the type of labor, the size of the baby and, above all, the ability of the physician in charge of that disaster.

In many elderly primigravidas, a section is surely justified, but the mere fact that the patient is older than many women having their first babies is no good indication. The size of the baby, its relation to the pelvis and the condition of the cervix are determining factors. If the decision is to operate, an elective section should give the best results. This year, 2 mothers in this group were lost following emergency sections.

There seems to be no justification for doing a section simply because the patient is young (fourteen), unless there is some definite indication.

The advisability of operating because of fetal distress has been consistently questioned. More justifiable, if conditions are good, is operation for a prolapsed cord when the cervix is not fully dilated.

Regarding the indication, "following operative attempts," it should be repeated that at best this is a dangerous procedure. Of the 8 cases so classified, 4 followed the unsuccessful application of

forceps. Three of these patients had stormy convalescences. One, on whom a Waters section was done, made a good recovery. One baby was lost. Three patients had malformed babies, 1 being a double-headed monstrosity. In this case, the questionnaire states: "Forceps tried and failed, then decapitation and attempted forceps on the other head, followed by attempted version and extraction. Finally a cesarean section of the peritoneal exclusion type was done. After a very stormy convalescence, the patient recovered." It is obvious from the questionnaire that this was a most difficult case to manage, and the operator was fortunate that the patient did not die.

Two fetuses were hydrocephalic. It is stated in one case that a craniotomy was done, but since the head did not engage, a low section was performed. The obstetric judgment in not completing the delivery following craniotomy is open to question. In the other case, the note states, "Attempted breech extraction to mid thigh; delivery failed, and a section was then done." This case is considered under the maternal deaths.

The next indication, "for sterilization or by request," cannot be considered justifiable.

Four cases are recorded under "ruptured uterus," 2 being spontaneous and 2 following previous sections. These cases were so diagnosed. There were, however, 6 others that were discovered at operation following previous sections.

The indication, "postmaturity," is questionable, especially when the questionnaire says "one week overdue." In 1 case, the patient was stated to be two and one-half weeks overdue, with a large abdomen; a section was done, and twins were delivered. The mother died. The case is commented on below.

With a known malformation of the fetus incompatible with life, cesarean section is not justifiable without other indication.

In 3 cases, the only indication given was "twins." In 1, the pelvis was reported as rachitic. In this case, the babies weighed 6 pounds, 8 ounces, and 6 pounds, 4 ounces. There were 18 other cases of twin pregnancy and 1 case of triplets, but these were all assigned to other indications than "multiple pregnancy."

In 3 cases, the only indication given was "floating head (patient not in labor)." There was no note of the relation of the size of the head to the pelvis, or whether the patient was approximately at full term. That a floating head can be regarded as an adequate indication is doubtful.

The indication, "Varicosities," is also open to criticism, unless the condition is very severe.

The 19 cases classified as "Bizarre" need not be taken up in detail. Several were classified as "dys-

tocia," although the patients were not in labor. In 2 cases, the only indication was "multiparity." One baby weighed 6 pounds, 11 ounces, and the other weighed 7 pounds, 11 ounces. In another case, it was stated that the patient had "soft-tissue dystocia," and yet there was no labor. In another, the only indication was "necessity for pelvic operation." One indication was, "Severe persisting labor for three days; fainting spells, with vomiting; question of concealed hemorrhage." A section was done, and the baby, in good condition, weighed 7 pounds, 9 ounces.

One indication given was:

The following sociological condition: The patient was living with her husband's family, with no opportunity to go on her own. The family were very critical of her repeated pregnancies, this being her third. Because of this and the facts that she had a third-degree tear with a good repair, that she was very desirous of having her tubes tied off, and that the baby was a large one, a cesarean section was done.

Another indication was a "fixed cervix." What that means, I do not know. There was no labor. The baby was born dead. There was 1 case of "locked twins." In the final case, a classical section was done because "the vagina had been explored at six months." The patient had no labor. The baby weighed 6 pounds, 12 ounces.

There were 63 cases in which no indication was recorded. Doubtless, the indications were good and sufficient, but the questionnaires did not show them.

Table 6 presents a summary of the 41 maternal deaths that occurred in 1940. Deaths from emergency sections are always more frequent than

thrombosis of the superior mesenteric artery, 1 from embolus, and 2 from hemorrhage.

In the first of the 2 deaths from hemorrhage, autopsy revealed a most unusual condition. The patient had had five previous sections. At this operation, a low transverse section was done. At the time of operation, it was noted that the previous incisions were covered by large varicosities. The patient was returned to the ward in good condition. Four hours later, she suddenly went into shock. In spite of transfusion and stimulation, she died. At autopsy, the abdominal cavity contained much blood and one clot the size of a grapefruit.

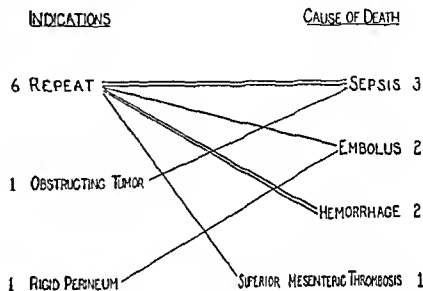


FIGURE 1. Maternal Deaths in 8 Elective Cesarean Sections.

The old scar was gaping wide open, but the new scar was intact. There is no note regarding the varicosities.

In the other death from hemorrhage, the cause given on the death certificate was "shock due to cesarean section." On investigation, it was found that because of excessive loss of blood at the operation the patient was in poor condition. The operator, a general surgeon, left immediately after the operation. In the absence of the operator, treatment consisted in the administration of stimulants.

Two cases were assigned to embolus. I wish to comment on 1. In the questionnaire, the indication for the section was "contracted pelvis, rigid perineum and narrow introitus." Convalescence was normal, and at the end of fourteen days, the patient was about to be taken home when she complained of severe exhaustion and weakness. She suddenly expired from an embolus. It was reported by the investigator who looked up this death that the patient had a transverse position with knee and elbow presenting. On the tenth day, she was up and about to go home when she felt faint and weak and was put back to bed and kept there for two weeks longer. She was about to be transferred by ambulance when she suddenly died. This patient probably did die from an embolus.

TABLE 6. Summary of Cases with Maternal Death.

DATA	NO. OF CASES
Emergency operation	33
Elective operation	8
Type of operation:	
Low	15
Classical	20
Waters	2
Porro	4
In labor	22
Not in labor	19
Membranes ruptured	17
Membranes unruptured	24
Babies:	
Living	36
Dead	8

those from elective sections. The situation in 1940 is unchanged. The number of deaths following elective sections (8) is the lowest that has been recorded.

The other figures need no comment.

Figure 1 shows the indications and the causes of death in the elective sections. There were 6 repeat sections: 2 patients died from sepsis, 1 from

but the history as given in the questionnaire and the story as obtained by the physician who investigated the death show so great variance both in the indications for operation and in the convalescence that it seems worth noting.

The cause of the final death under elective sections was given as "obstructing tumor." This patient died of sepsis.

Figure 2 shows the indications and the causes of death in the 33 emergency sections.

Ten patients were classified as dying from sepsis. Seven of these were so diagnosed on the death certificate. Of the other 3, one was reported on the questionnaire as dying from bronchopneumonia,

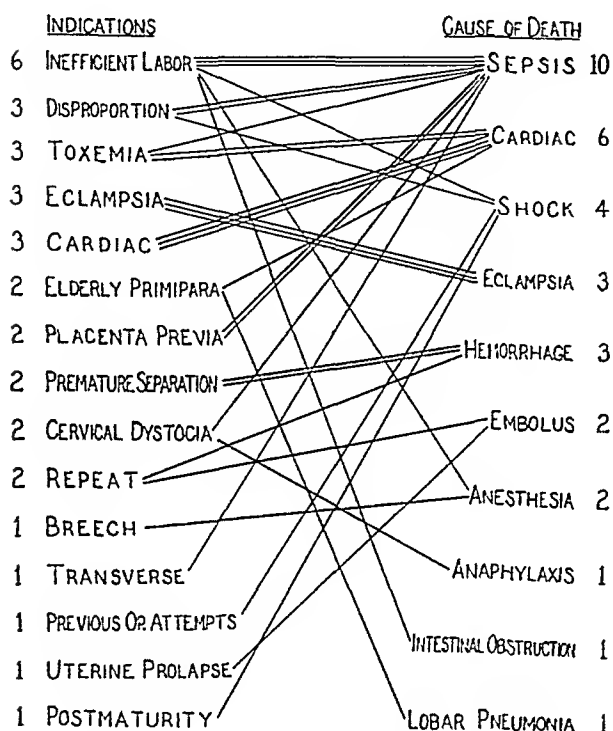


FIGURE 2. Maternal Deaths in 33 Emergency Cesarean Sections.

and another from embolus. The third is considered below. Autopsy on the first of these showed multiple abscesses of the uterine wall and multiple pulmonary emboli. The second patient ran a temperature of 100 to 101°F. each day after the operation. At autopsy, a thrombosis of the pelvic veins was found. This patient undoubtedly had an embolus, but she was also septic and was therefore so classified. Possibly, this death should be classified as due to embolus.

The third case deserves comment. The indication for operation as given in the questionnaire is as follows: "The patient was a para III. Examination showed uterine inertia, primary and secondary; uterine anomaly, nonpathologic; cardio-renal disease; pre-partum toxemia; uremic syn-

drome; and pernicious anemia." The questionnaire states that a classical section was done; the membranes were not ruptured, and the patient was in labor fifty-two hours. The causes of death were given as follows: "pregnancy, uterine inertia, pernicious anemia, post-partum toxemia, intestinal obstruction and circulatory failure."

The investigator's note is as follows:

The patient ran a postoperative temperature of 103 to 105°F. There was no indication of pernicious anemia by signs, symptoms or laboratory study. A low section was done following a twenty-four-hour labor, with full dilatation for four hours. The doctor who operated stated that the membranes were unruptured but bulged out through the vagina. He saw something in the front part of the vagina that he designated "nonpathologic uterine anomaly." The patient had had two normal deliveries.

This patient obviously died of sepsis. The case was misdiagnosed and mistreated throughout. Death must be laid at the door of the physicians and of the hospital that allows such men to carry on.

The indications for the section in 10 patients who died of sepsis were: inefficient labor, 3; disproportion, 2; toxemia, 1; placenta previa, 2; so-called "cervical dystocia," 1; and transverse presentation, 1. In this group, 5 classical sections were done, 4 being of the low and 1 of the Waters type.

It seems poor judgment to do a classical section on a woman who has been in labor many hours with ruptured membranes. The risk that such an operation entails has been established for many years.

Four deaths are classified as due to shock—1 following inefficient labor, 1 with the patient in labor for twelve hours with disproportion, 1 in which an operative attempt failed and 1 with the questionable indication of "postmaturity."

It is interesting to go a little farther into these cases. In the first, the indication was a long labor with a high presenting part and no dilatation of the cervix. The length of labor was not stated. But the physician who investigated the case found that the patient was in labor sixteen hours without progress, that she died four hours after operation and that she was transfused three times.

The second patient died three hours after operation. On the questionnaire, there was no further comment, but it was discovered by the investigator that she had received 21 gr. of Seconal within twelve hours, and it was believed that this large amount of Seconal had something to do with the death.

The case in which operative attempt failed needs explanation. The indication given on the questionnaire was, "On attempted breech extraction to

the midhigh, it was impossible to deliver the child; therefore, a section was done." The patient died of shock an hour after leaving the operating room, and the baby was stillborn. On investigation, the following facts were elicited. The patient had eight living children. The present baby was not of excessive size. The patient had a twenty-four-hour labor, with ruptured membranes. Many vaginal examinations were made. Delivery by forceps was attempted three times, followed by an attempted version and extraction. All this was done previous to a classical section.

In the case in which the indication was given as "postmaturity," it was stated that the patient had a very large uterus and that she was two and one half weeks overdue. The physician tried to induce labor with quinine and castor oil, without effect. The patient was in labor twelve to fourteen hours, when a section was done and twins were delivered, one weighing 5 pounds, 13 ounces, and the other, 5 pounds, 8 ounces. The operation was done by a general surgeon, and there is no record that an x-ray examination was made. There seems no real indication for this section. The patient failed very quickly after leaving the operating room and died soon afterward. The twins left the hospital in good condition.

Six deaths are classified as due to cardiac conditions. Two of these patients were known to have had cardiac conditions during pregnancy. Another was found moribund, supposedly because of a bad heart condition, having had no medical care whatsoever, and the physician did an emergency section in the home without previous preparation, with the hope of obtaining a live baby. The baby was stillborn.

In still another case, the patient was a forty-four-year-old primipara, who apparently had acute cardiac decompensation with pulmonary edema shortly after operation.

Two sections were done because of toxemia, one very severe and the other mild. The latter patient had triplets. She went to pieces shortly after the operation and died in spite of all stimulation. The three babies lived. The other patient was a Christian Scientist who had had no satisfactory medical care. She developed a congestive heart failure while in labor and was digitalized; a section was done under local anesthesia. The baby died.

There is nothing to be said of the 3 eclamptic deaths, except that a section is not at present regarded as good treatment in such cases. The 3 babies survived.

In the 3 cases of hemorrhage, 2 sections were done for separated placenta. In the first of these, the patient had been bleeding off and on during the entire pregnancy. She was hospitalized at the

seventh month and kept in bed for three weeks until it was thought that the baby was viable. At operation, she bled very profusely, and continued to bleed after the section was completed. She was transfused during the section and five times thereafter. An hour after operation, a hysterectomy was done. The baby did not survive. In the other case of separated placenta, the patient oozed from the arm where blood had been taken, and at the operation the uterus failed to contract satisfactorily. Four hours after operation, a hysterectomy was done while she was in very bad shape, and she died half an hour later. She was given a total of 3000 cc. of blood. These 2 cases show the necessity, when the uterus fails to contract, of doing a hysterectomy at once instead of delaying until the patient is in a desperate condition.

The third death was due to placenta previa and placenta accreta. This patient had been in bed at home for three weeks with a small amount of staining of pinkish fluid. She suddenly had a tremendous hemorrhage, and a section was done. As soon as the accreta was diagnosed, a supravaginal hysterectomy followed, but the bleeding continued. The patient died on the table. The baby did not survive.

I have classified 2 deaths as caused by embolus. One followed a repeat section. Following the operation, which was of the extraperitoneal type, the patient ran a fever. She was thought to be in satisfactory condition to go home when she suddenly had an embolus and died. Autopsy showed that there was a small amount of pus at the lower end of the abdominal wound and a thrombosis of the right iliac vein. This patient in all probability had a low grade sepsis.

The other case of embolus needs a little elaboration, for the questionnaire and the report given on investigation of the death are at variance. The questionnaire states that the indication was toxemia of pregnancy due to a nephritic condition, with vaginal bleeding. A classical section was done. An uneventful recovery from anesthesia followed. On the sixth day, the patient had an embolus and died. On investigation, the following facts were discovered. The patient had had two previous normal pregnancies. During this pregnancy, she had had slight irregular spotting. There was no bleeding on entrance or before the operation. The patient was hospitalized at the seventh month, and the hospital record states that there was an existing uterine prolapse. The surgeons in this hospital elected to operate and did a Porro section at seven months. The patient did die from an embolus, but the necessity for the operation is more than questionable.

Two cases are classified as due to "anesthesia"

In one, the indication was a breech, and in the other, inefficient labor. In both cases, the cause of death was given on the questionnaire as pulmonary embolus, but in each case the patient was cyanotic throughout the anesthetic, with a large amount of mucus and frequent vomiting. There is no doubt that both patients had pulmonary edema, and possibly acute dilatation of the heart, but the underlying cause of death was a poorly given anesthetic.

In the next case, in which the section was undertaken because of anaphylaxis, the physician stated in the questionnaire that the death was due to misgrouping. That, of course, may be true, but the question arises whether this death was not connected in some way with the recently discovered Rh factor.

In another case, intestinal obstruction may have been the correct cause of death. The cause as given in the questionnaire was "intestinal stasis, probable ulcer of the stomach." The patient had had three previous abdominal operations. The investigator found that she had given a history of chronic indigestion for several years. She had had vomiting and abdominal pain when seven months pregnant. She vomited a good deal after the operation. At operation, many adhesions were found, and the investigator believed that the death was

in all probability due to intestinal obstruction, which was incomplete at the beginning and later became complete.

The indication for the last case, in which the cause of death was lobar pneumonia, was "elderly primipara." The patient was in labor for some hours. The questionnaire states that she developed lobar pneumonia and cardiac failure and died on the fourth day. No further information is available regarding this case.

It is difficult to say how many of these deaths were preventable, but I think it will be agreed that the number of deaths was greater than it should have been. There were 219 maternal deaths in Massachusetts in 1940, giving a death rate of 2.8. But it must be noted that cesarean section figured in nearly 19 per cent of the deaths. There is no doubt that the results obtained were remarkably good. However, the fact remains that altogether too many sections are being done.

In 1940, there was a greater variance between the statements on the questionnaires and the facts elicited by the investigators. It was obvious in some cases that the questionnaires covered up the actual causes of death and the indications for operation.

330 Dartmouth Street

THE TREATMENT OF PSORIASIS WITH A SARSAPARILLA COMPOUND*

FRANCIS M. THURMON, M.D.†

BOSTON

SARSAPARILLA has been used as a medication since 1603, when Martin Pring,¹ in the English ship *Speedwell*, searched the New England coast for forests of sassafras, which then was considered "a panacea for all manner of disease." In America, the earliest colonial settlers purveyed sarsaparilla as the inevitable spring tonic, attributing to its use a diuretic, diaphoretic, tonic and alterative effect. By 1892, Schulz² recognized the fact that there were different varieties of this dried root of the *Smilax* species and believed that he had isolated three distinct saponins from sarsaparilla: parillin, sarsasaponin and smilasaponin. Since the observation of Schulz, a voluminous literature on the saponins has accumulated. It is the water-soluble saponin called sarsasaponin (parillin), obtained from the Honduras variety of sar-

saparilla, that forms the active ingredient of the tablets used in this study.

A survey of the literature, covering fifty-two original articles, on the chemical composition of the various types of sarsaparilla, the nature of the saponins and the structure of the sapogenins reveals that only one definite saponin has been isolated from any of the varieties of sarsaparilla. This compound is generally called "sarsasaponin (parillin)." Its chemical constants are: melting point, 238 to 240°C. (Van der Haar³) and formula, $C_{45}H_{74}O_{17}$. On hydrolysis with dilute acid, it yields one molecule of sarsasapogenin (parigenin), two molecules of glucose and one molecule of rhamnose. The Honduras and Mexican varieties apparently contain no other saponins.

In sassafras and various other plants distributed throughout the botanical realm, one finds a group of compounds referred to as the "digitalis saponins (and sapogenins)." These digitalis saponins, of

*From the Department of Dermatology, Tufts College Medical School, and the Clinic of Dermatology and Syphilology, Boston Dispensary.

†Assistant professor of dermatology, Tufts College Medical School; physician-in-chief, Clinic of Dermatology and Syphilology, Boston Dispensary.

which sarsasaponin is one, are not to be confused with the "cardiac glycosides" obtained from digitalis plants. The term "digitalis saponins" is purely a chemical classification, and a confusing one at that. Chemically, the two substances are sharply differentiated. Each has quite different and characteristic side chains. The digitalis saponins have none of the physiologic action on heart muscle that characterizes the cardiac glycosides, which also contain unusual sugar molecules not found elsewhere in nature. A still further differentiation lies in the ability of the digitalis saponins to hemolyze erythrocytes in very low concentrations. The sarsasaponin product used in this study is prepared from a particular sarsaparilla and embodies no possibility of contamination with the digitalis cardiac principle; furthermore, the standardization of this sarsasaponin compound by the hemolytic index serves so completely to control optimal quality and uniformity of composition that hemolysis does not present a problem.

Ransom,⁴ in 1901, in an out-moded way, demonstrated a chemical affinity between the saponins and serum cholesterol by which the saponins acted on tissues without causing hemolysis. This affinity of saponins for cholesterol led Dencke,⁵ in 1936, to utilize the studies that Grutz and Burger⁶ had completed three years earlier. Grutz and Bürger found that patients with psoriasis (as compared with nonpsoriatic persons, showed an increase, respectively, in total blood fat of 44 per cent, cholesterol 33 per cent, and phosphatides 43 per cent. Following this, they naturally restricted the fat intake of patients with psoriasis. Dencke advanced farther, by supplementing the fat-deficient diet with the oral administration of sarsaparilla, hoping to utilize the chemical affinity of the sarsaparilla saponin for cholesterol. This procedure met with some success.

Not all patients with psoriasis, however, have a disturbed lipid metabolism. Hering,⁷ in 1938, duplicating the work of Grutz and Burger, observed that the phosphatide content of the blood approached normal levels, and that the free and esterified cholesterol showed no significant deviations from normal. Hering did not believe a relation existed between psoriasis and a disturbed metabolism of fats. Rosen et al.,⁸ in 1937, concluded that the psoriatic process involves hypcholesteremia rather than hypercholesteremia; moreover, on the basis of cholesterol tolerance tests, the author asserted that it is not possible to assume that a disturbance of lipid metabolism is present in patients with psoriasis. Grubb,⁹ in 1935, assuming psoriasis to be a deficiency disease in which the vitamins of animal fats were lacking, prescribed a diet rich in butter (fat) for 3 patients

in whose diets butter had been previously prohibited, and the psoriasis disappeared in a short time. Madden,¹⁰ in 1939, using cholesterol tolerance tests, observed that hypercholesteremia did not generally exist, but that a low-fat diet was of definite value in 68 per cent of cases tested. Madden's patients were hospitalized. He inclined to the belief that the favorable effect of diet might be explained on the basis of a general realignment of metabolism, rather than because of the correction of a disturbed fat metabolism. He asserted that sarsaparilla, because of its saponin content, has an especial affinity for cholesterol and that its ingestion tends to restrict excesses. Stewart et al.,¹¹ in 1939, observed in 6 cases of psoriasis, that 3 patients had lipemia, 2 had blood lipid values within normal range, and 1 showed subnormal values. Despite these conflicting observations, Wise and Sulzberger¹² state that there is no doubt that certain cases of psoriasis are much improved by a strict "fatless" diet. Their special article on psoriasis and its treatment is an excellent contribution, and should be read by all who are interested in this disease.

To Philippsohn¹³ should go the credit for modernizing the old observation that sarsaparilla possessed value as a medicine. His successful use of sarsaparilla in the treatment of psoriasis is interesting. Patients were instructed to make their own compound into 1000 cc. of tepid water, 15 gm of sarsaparilla was placed. This was done in the afternoon, and the mixture was allowed to stand overnight, and then boiled for twenty minutes the following morning. While the mixture was still hot, the patient drank half the liquid that morning, the remainder being consumed during the afternoon of the same day. Usually after a week of this daily procedure, decreased desquamation occurred, which, after its complete disappearance, was marked by a smooth red macule that eventually faded. Philippsohn noted no untoward effect from sarsaparilla. One patient who had used the mixture daily for twenty years failed to experience a single relapse of a previously stubborn psoriasis.

Ritter,¹⁴ using the sarsaparilla tablets of Burger, treated 19 private patients. Ten tablets were administered daily. Nine patients became completely or nearly completely free from psoriasis. The shortest required duration of treatment was two weeks, the average period being sixty to one hundred days. Five cases showed improvement but did not completely clear. Five patients showed no improvement at all. On the 10 patients without satisfactory response, Ritter also used a low-fat diet, bland ointments, salicylated vaseline, precipitates and chrysarobin. No harmful or toxic effects were observed.

Zaun,¹⁵ in 1938, treated 20 cases of psoriasis, using five to thirty sarsaparilla tablets daily, a low-fat diet and a salicylated ointment locally. Satisfactory results were obtained in all cases except a few in which the patients failed to follow treatment as advised.

Wise and Sulzberger¹² describe the use of sarsaparilla tablets as a treatment for psoriasis. Baird¹⁶ comments conservatively on the results obtained in 6 cases treated with sarsaparilla.

With an appreciation of the facts as outlined above, there appeared a certain logic in the thought that the standardized, nontoxic, water-soluble fraction of sarsaparilla (sarsasaponin) should possess virtues in the treatment of psoriasis. The present communication is a report of such a study.

CLINICAL MATERIAL

This clinical study covers the past two years. A two-year period was deemed necessary because of the desirability of studying the effectiveness of sarsasaponin tablets on the seasonal variations of psoriasis and its efficacy in controlling recurrent eruptions.

Ninety-two patients were studied. Of these, 75 were treated with the sarsasaponin tablets, and 17 were used as controls. Twelve additional cases were started, but failed to continue a sufficient period to merit inclusion in the series. There were 53 females and 39 males, a ratio of 1.3:1. The average age of onset was twenty-nine years. The youngest patient was three years of age, and the oldest seventy-six. The earliest age of onset was infancy, and the latest sixty-seven. The average duration of psoriasis was ten years, the shortest being three weeks, and the longest fifty-two years. Thirty-seven patients had psoriasis ten years or longer.

A history of familial incidence was obtained in 15 cases (16 per cent). The parents of 5 patients had psoriasis. In contrast, 53 (20 male and 33 female) were the parents of 121 children, and in no case did psoriasis appear in their progeny. This observation indicates clearly that psoriasis is not a deterrent to marriage and the begetting of progeny. Third-generation psoriasis was not noted. The patients were American, English, Canadian, Scottish, Irish, Swedish, Russian, Lithuanian, Portuguese, Jewish, German and Italian.

Objectively, the lesions were of the type and distribution generally described as psoriasis vulgaris. Arthritis or rheumatic joint disease was present in 13 cases (14 per cent). There were no cases of psoriasis pustulosa. Characteristic polymorphism of the lesions was apparent. Large plaque-type lesions were present in 42 per cent. Expressed in percentage, the following areas were involved: scalp, 74; trunk, 60; elbows, 60; knees, 53; nails, 32; genitals, groins and gluteal crease, 36.

The subjective symptoms of itching and burning at one stage or another were unusually frequent, being present in 68 per cent of the cases. Nervousness, a tendency to worry, and vasomotor instability, which, when acute, accentuated pruritus and frequently stimulated the appearance of new crops of lesions, were noted in 36 per cent. A seventeen-year-old boy, brooding over his psoriasis, made four attempts at suicide. One patient, on the death of her husband, quickly developed a fresh exanthematous spread of new lesions. One patient, a student at a local university, was also a student aviator. Owing to storms and bad weather, there was no flying in February, and his psoriasis began to clear. Then came the time for his first solo test flight. Apparently, the nervousness and excitement in anticipation of this examination proved sufficiently stimulating to cause improvement of the lesions to cease, and his psoriasis became quite active and more widespread.

There were several examples of polysensitivity among these cases, such as asthma, hay fever, urticaria and eczema, which had occurred in antecedent members of the patient's families, although a family history of psoriasis was not necessarily present.

The histories in 85 per cent revealed a distinct tendency for the psoriasis to improve during the warm summer months. All patients were warned about overexposure to the sun, yet, in 5 cases of severe sunburn, fresh outbreaks of punctate, guttate or nummular lesions occurred. In New England, the predominant periods for recurrent eruptions are September and October, and March and April, whereas during the winter, when skins and scalps are dry, nails are brittle, and seasonal keratotic follicularis is marked, the psoriatic patient is hard pressed. The patient with psoriasis apparently has a peculiar inherent physiologic habitat on which any number of factors and circumstances may prove stimulating, and when present in sufficient force the inevitable cutaneous response is one of psoriasis.

In all cases, syphilis was ruled out as an etiologic factor, either by treatment or by physical examination and negative Hinton, Wassermann and Kahn reactions of the blood. In 4 cases in which syphilis was present, it was of the tertiary type, and treatment did not influence the psoriasis, except occasionally to produce an accentuation of the lesions. A careful check was kept on the renal status and the hemoglobin and blood counts all through this study. In no case was there evidence of renal irritation. Blood counts performed before, during and following treatment with the sarsasaponin tablets failed to reveal evidence of hemolysis. Three patients showed a rise in hemoglobin from 10 to

15 per cent. The erythrocyte count either held its level determined prior to treatment, or showed an increase of as much as 750,000 cells. The leukocyte count seemed unaffected. The differential counts were not remarkable except for a fairly consistent though mild eosinophilia. The blood smears invariably revealed a goodly number of platelets in all preparations.

TREATMENT

Dosage

It is essential that the sarsasaponin tablets be taken regularly. It is advisable, at the start, to prepare the patient for a three to seven months' course of the medication. If a shorter period is required, so much the better.

The usual adult dose is one tablet* twice daily, preferably taken with a warm liquid at a time when the stomach is likeliest to be empty. These two periods are the early morning on arising and the last thing at night before retiring. A larger dose, two tablets twice daily, or even two tablets morning and evening and one at noon before luncheon, may unhesitatingly be administered. For children aged five years or under, half a scored tablet given twice daily is sufficient.

A diet low in fat will prove beneficial for a large number of patients. Liquids in the amount of 1500 cc. or more daily are recommended.

It should be stated that, for the purpose of this investigation, the tablets used were less concentrated than those that are commercially available at present. A single tablet of the dosage described above contains the equivalent amount of sarsasaponin contained in five of the tablets used in the clinical evaluation. This concentration of the active ingredient of five of the old tablets into one of the new tablets was considered advisable merely as a convenience for the patient. The new tablet is scored; the smaller and older tablet is not. All statements regarding the sarsasaponin tablets in this paper, therefore, apply to the smaller, older tablets of weaker strength. Its equivalent in new tablets may be obtained by dividing by five.

Local Therapy

During the first twelve months of this study, no diet or topical applications were prescribed. During this period, it was shown that the tablets were nontoxic and therapeutically effective. With these two points cleared, there could be no logical objection to a local therapy designed to hasten involution of the lesions, provided that this therapy was not irritating. Consequently, a variety of topical applications were used. They comprised, chief-

ly: irradiation in the form of sunshine or ultraviolet lamp, boric acid ointment, lanolin, petrolatum, olive oil, mild precipitate ointments, salicylic and sulfur preparations, and modified coal tars. Of these, the most effective agents were irradiant energy and a modified coal-tar preparation, Ultrone Ointment.[†] This ointment is a clean, gray to white, nonirritating preparation, which has as its active ingredient the distillate of coal tar. The 2.5, 10 and 20 per cent concentrations proved exceedingly beneficial as a topical application twice daily. One can state definitely that the oral administration of the sarsasaponin seemed to enhance the effectiveness of treatment locally.

RESULTS

Table I shows that in the group treated with the sarsasaponin tablets there was a satisfactory improvement, as compared with the condition of the controls. By combining the results of moderate and marked improvement, the percentage that may be considered good was 62. Eighteen per cent of cases

TABLE 1. Results of Treatment with Sarsasaponin Tablets.

RESULTS	TREATED CASES NUMBER OF PATIENTS	PER- CENT- AGE	CONTROL CASES NUMBER OF PATIENTS	PER- CENT- AGE
Clearance (100%)	14	18	1	6
Marked improvement (75%)	16	21	1	6
Moderate improvement (50%)	17	23	2	12
Slight improvement (25%)	12	16	3	18
No improvement	14	19	7	41
Exacerbation of lesions	2	3	3	17
Totals	75		17	

cleared completely. The data on improvement compares favorably with Ritter's¹⁴ experience in 19 private patients treated with the sarsaparilla tablets of Bürger. Nine of Ritter's patients (48 per cent) became completely or nearly completely free of psoriasis, 5 (26 per cent) showed some improvement, and 5 showed no improvement.

In the 14 cases that cleared, the average period of treatment was four months; the shortest period was four weeks, and the longest seven months. The average period of remissions was eight months, the shortest being three months and the longest twenty months. An analysis of these cases reveals that the greatest clearing occurred during the late spring and summer (Table 2). The experience of two full summers showed no photosensitive effect from the sun. As a matter of fact, there is a distinct impression that the tablets enhance the effectiveness of mild sunshine.

Forty per cent of the patients showed moderate or marked improvement. Most of them also

*The sarsaparilla (Sas Par) tablets used in this study were supplied by First Bischoff Company, Incorporated, Ivoryton, Connecticut.

†This mixture is manufactured by Lamy Chemicals, Incorporated, Boston.

showed the greatest benefit during the warm summer months. This cannot be entirely attributed to the direct effect of the sun's rays, because many of the patients had indoor occupations and little or no opportunity for beach or sun bathing. There is something about the warmer seasons of the year that is beneficial to psoriasis.

Recurrent eruptions most commonly appeared in the fall, winter and spring. Although the administration of this sarsaparilla saponin did not completely control these recurrences, their intensity was considerably modified and less severe as compared with similar periods of cold weather during

TABLE 2. *Analysis of 14 Treated Patients Whose Psoriasis Cleared.*

TOTAL PERIOD OF TREATMENT MONTHS	NO OF TABLETS REQUIRED	PERIOD OF TREATMENT	RECURRENCE OF PSORIASIS	LENGTH OF REMISSION MONTHS
1	225	February	January	11
2	525	June-August	May	9
2	600	June-August	December	4
2	825	April-June	None	10
3	600	October-January	July	6
3	975	February-May	September	4
3½	525	April-July	None	12
4	1425	February-June	October	4
4	1800	February-June	February	8
5	1650	November-April	None	20
5½	1650	February-July	December	5
6	1250	May-November	None	3
7	2325	October-May	September	4
7	2416	November-June	None	18

preceding years. The dissemination of the eruption was less widespread, its course was milder, the response to local therapy was better, and itching was not nearly the uncomfortable factor that it had usually been. In many cases, the control of pruritus was dramatic. In others, itching was intense, regardless of what was used.

Of the 13 cases of arthritis or rheumatic joint disease and psoriasis, nothing definite can be said about relief of pain. One patient, a sixty-six-year-old man, had painful arthritic involvement of the wrists, hands and right ankle; he received 2925 sarsasaponin tablets over a nine months' period, and it was not until the last three months (October, November and December) of treatment that relief from pain and improvement of the psoriasis were obtained. A forty-three-year-old woman had severe generalized psoriasis including the scalp and nails, and nodular painful arthritic deformities of the hands. She took 5900 sarsasaponin tablets for twenty-one months. The arthritis and psoriasis, including the scalp and nails, were markedly improved. She gained weight, the psoriasis underwent two almost complete remissions, and during the past winter her arthritic pains and psoriasis were so slight as not to be noticeable. She continues to take the sarsaparilla tablets. Another patient, a seventy-six-year-old woman, had painful

arthritis and a chronic, generalized, plaque and papular psoriasis of twenty-two years' duration. The scalp, nails, genitals and gluteal crease were also involved. Her greatest relief was obtained from the sarsasaponin medication. In twenty-two months, this patient took 6075 tablets, and, although the psoriasis was not completely controlled, improvement was moderate, and she continued to take the sarsaparilla compound. In contrast to these favorable impressions, there were similar cases in which the arthritic pains and psoriasis continued apace despite the saponin medication.

Twenty-six cases (35 per cent) of the series showed slight to no improvement, and in 2 (3 per cent) the psoriasis was distinctly accentuated. Thus, in 38 per cent, the response was not favorable. In the light of present knowledge, no adequate explanation for this failure may be advanced. The average period of treatment was three months, and the average number of tablets administered was 942. If this group is contrasted with the successful cases, which required an average of four months to establish a remission, a fair trial period of the tablets is three or four months.

A typical case with complete remission is that of a thirty-two-year-old man. His psoriasis was of eighteen years' duration and generalized—in fact it was so severe that he went outside only at night. There was slight improvement from sun bathing and the use of an ultraviolet lamp, but at no time was there complete clearing. In November, 1939, the patient began sarsasaponin, taking five tablets twice daily. A low-fat diet was advised, and no local therapy was prescribed. Within two weeks, there was a noticeable reduction in the eruption, and pruritus was controlled. The dosage was increased to eight tablets twice daily. Within the next four weeks, the scalp was greatly improved, the scalp hair regained a natural waviness and luster, and the previously extensive eruption on the face was indicated only by erythematous macular patches. Within ten weeks from the start of this medication, only a few patches of psoriasis remained on the arms, chest and thighs. In February, a slight exacerbation of the eruption occurred. At this time, the patient had been without the tablets for a week. On resumption of sarsasaponin, the new lesions quickly vanished, and favorable progress, although slower than at first, was steady. By June, 1940, seven months later, there was no trace of the psoriasis. All areas, including the scalp, groin, elbows and knees, were completely clear.

The effect of a low-fat diet seemed to be helpful. Twenty-four patients were advised to eat as little fatty food as possible during the period of treatment. Of these, 50 per cent showed marked im-

provement, and 16 per cent, complete clearing, whereas the remaining 34 per cent were either slightly improved or less. There can be no doubt that certain cases of psoriasis are improved by the use of a low-fat diet.

The results attained by the use of the saponin of sarsaparilla were superior to those with the usual procedures commonly applied in the 17 patients used as controls. Table 1 amply illustrates this point.

The control cases received dietary management, local treatment, such as Alpine sun lamp, cold quartz ultraviolet radiation, sunshine and ointments of various kinds, including salicylic acid, sulfur, precipitates and coal and wood tars, colloidal manganese, bismuth and liver extract intramuscularly; arsenic in the form of Fowler's solution; and vitamins A, D and B complex orally.

DISCUSSION

The results attained in this series of 75 treated cases of psoriasis were neither remarkably successful nor disappointing. They were far better than average. In certain cases, they were brilliant. Emphatically, sarsaponin is worthy of clinical trial in any case of psoriasis. No toxic systemic effect from its use was observed. A careful check on the cardiovascular, renal, gastrointestinal and hematopoietic systems failed to reveal any untoward reaction. In contrast, many of the patients developed increased appetite, gained from 4 to 12 pounds in weight, and seemed less nervous, slept better and experienced less itching. Three women took the sarsaponin during pregnancy without ill effect, and their psoriasis simultaneously improved.

One distinct impression regarding sarsaponin therapy is that the drug has a greater value in clearing the chronic, large, plaque type of lesion than it has in controlling the recurrent evanescent and exanthematous punctate, nummular and guttate lesions. The individual new recurrent crops of eruption, in most cases, were milder, but they did appear despite the sarsaponin medication.

These cases gave rise to the impression that vasomotor instability, blond complexion and a tendency toward anxiety, worry and nervousness are not causative or even predisposing factors

to the occurrence of psoriasis, but that psoriasis runs a more recalcitrant course in a person possessing this triad.

The tragic and conditioning features of psoriasis on the behavior of this small group is illustrated by one suicide, one attempt at suicide, two adolescents with mental reactions of inferiority that led to strange and perverted behavior, several cases of refusal to marry, and numerous patients with neuroses because of their disfigured appearance.

SUMMARY AND CONCLUSIONS

A new drug, the water soluble saponin, called "sarsaponin (parillin)," obtained from Honduran sarsaparilla is described. The technique of its administration and its effectiveness in 75 patients with psoriasis are discussed. Seventeen additional cases served as controls. The study covered two years.

Observations from the literature concerning the nature of the sarsaparilla saponins and the influence of lipid metabolism on psoriasis are made.

When administered orally, the sarsaparilla tablets had a decided and beneficial effect on 62 per cent of patients with psoriasis.

520 Commonwealth Avenue

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A MECHANISM FOR SYNCOPAL ATTACKS ASSOCIATED WITH PAROXYSMAL AURICULAR FIBRILLATION

WILFRID J. COMEAU, M.D.*

BANGOR, MAINE

FROM a clinical standpoint, the mechanism of attacks of faintness or of actual syncope may be extremely obscure even after considerable study, since observation of the attack is often necessary to clarify the problem. In patients with rather infrequent attacks, such observation is entirely fortuitous unless they can be produced at will, and consequently the primary mechanism of the seizures usually remains a matter of speculation. Contrary to popular belief, organic heart disease is an uncommon cause of syncope, and such cases are confined largely to ventricular arrest due to interference with the conduction system as a result of coronary-artery disease and to the even rarer syncopal attacks associated with aortic stenosis or the shock of severe coronary insufficiency.

It is known that exaggerated vagal reflexes can cause functional disturbances in the regulatory mechanism of the normal heart, resulting in ventricular or complete cardiac arrest, and can thereby produce cerebral ischemia and syncope by a secondary lowering of the blood pressure. The sensitive carotid sinus, for example, at times acts in this manner to produce fainting. Furthermore, it is known that vagal stimulation may be a factor in precipitating auricular fibrillation.

It has been recognized for many years that faintness and syncope may be associated with attacks of the various paroxysmal arrhythmias. Although usually attributed to a drop in blood pressure consequent to the rapid ventricular rate, I believe the primary mechanism responsible for syncope in these cases has never been adequately demonstrated. The chance observation of the following case during a syncopal attack throws new light on a mechanism producing syncope in some of these cases.

CASE REPORT

G. H. B., a 40-year-old married male nurse, was first seen in February, 1941. Since 1932, his usual good health had been periodically marred by attacks of faintness or syncope followed by short bouts of palpitation and irregular heart action. While feeling well and for no apparent reason, the patient experienced attacks of faintness or loss of consciousness of several minutes' duration, following which he was aware of irregular heart action that ceased abruptly within 30 minutes to several hours. Other than causing some heart consciousness, the palpitation was not particularly uncomfortable and produced no ill effects. To the patient's knowledge, no convulsions had ever been associated with the syncopal seizures. These attacks usually

recurred for a day or so and then disappeared for periods varying from several months to several years. Since the onset, six or seven episodes had occurred, the last in 1938, following which the patient had consulted a cardiologist, who had found no physical abnormalities. Lumbar puncture, the Wassermann reaction, blood-sugar curves, the basal metabolic rate and electrocardiograms had always been normal.

The present episode, typical of those in the past, had started 36 hours previously, during which the patient had had several attacks of faintness and one attack of syncope. While the patient was being examined, he suddenly stated that an attack was coming on, and loss of consciousness gradually supervened, with progressively increasing ashen pallor, eyes at first staring and then rolling upward, and a cold clammy skin. The heart sounds, which had previously been audible and regular, ceased (no auricular sounds were heard), and asystole continued for at least 15 seconds, following which three or four slow irregular beats—at intervals of 2 or 3 seconds—were heard; gradually, an irregular rhythm was established at approximately 80 beats per minute, and consciousness returned. Afterward, the patient had no complaint except for irregular palpitation and a feeling of weakness. This bout of palpitation lasted about 3 hours and then ceased abruptly. When the patient was seen 3 days later, there had been no further attacks, and the attack observed was apparently the last of the present series.

The electrocardiogram taken during the irregular rhythm showed flutter fibrillation, with occasional ventricular ectopic beats at a ventricular rate of about 85 beats per minute (Fig. 1). The electrocardiogram taken 3 days later was entirely normal (Fig. 2).

Complete physical examination and fluoroscopic study of the heart and lungs several days after the attack showed no abnormality. The carotid sinus was not unduly sensitive.

It is of some interest that the sequence of events in this case parallels the findings of Iglaue, Davis and Altschule† and others who have induced auricular fibrillation in normal animals by vagal stimulation. It has been observed that auricular fibrillation, when produced experimentally by vagal stimulation, is not infrequently preceded by a short period of heart block; in a dog in which fibrillation was prolonged, the ventricular rate was slow. The ventricular rate of paroxysmal auricular fibrillation in human subjects is usually quite rapid (125 to 150), and it is therefore worth noting that in the case presented the ventricular rate averaged only 85 beats per minute. Exactly what type of heart block occurred is unproved, since good fortune did not extend itself to the point of allowing an electrocardiographic registration of this period.

†Iglaue, A., Davis, D., and Altschule, M. Auricular fibrillation in normal, intact animals after the intravenous administration of Mecholyl. *Am. Heart J.* 22:47-55, 1941.

*Cardiologist, Eastern Maine General Hospital, Bangor, Maine.

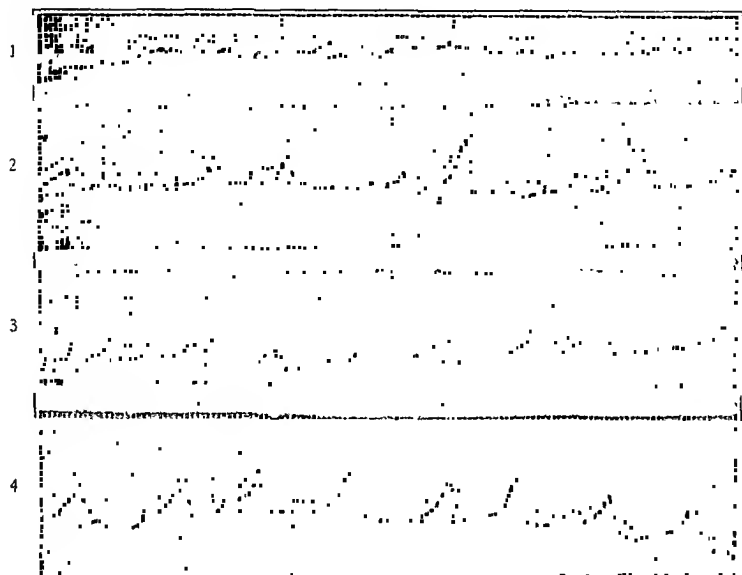


FIGURE 1. *Electrocardiogram during Paroxysmal Auricular Fibrillation.*

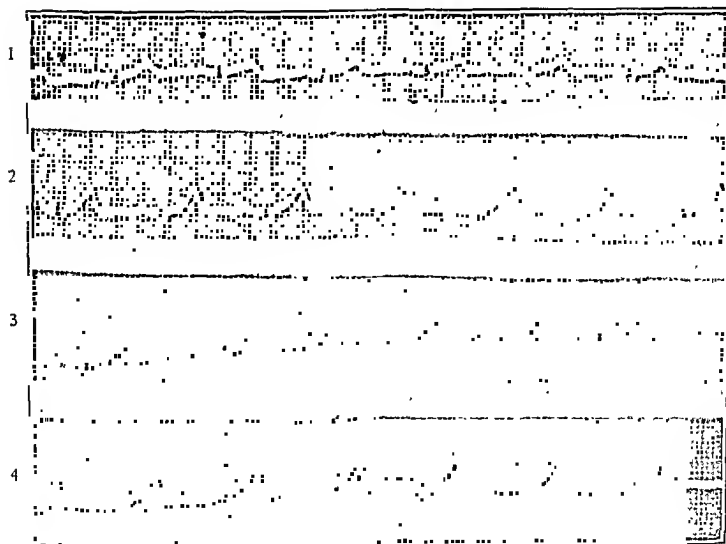


FIGURE 2. *Electrocardiogram during Normal Rhythm.*

It seems probable, however, that complete cardiac arrest (sinoauricular block) occurred rather than auriculoventricular block with only ventricular arrest. In any event, it seems but a short step from cardiac standstill caused by a vagotonic influence to auricular fibrillation due to the same mechanism.

DISCUSSION

It is also of interest to carry to the auricles the analogy of the events known to occur in the ventricles during Adams-Stokes seizures associated with complete auriculoventricular block, in which syncopal seizures are likeliest to occur during the paroxysmal stage of complete heart block; once the block is permanently established, the fainting attacks usually disappear. It has been shown electrocardiographically that there is frequently a latent period, with complete ventricular arrest and a syncopal attack, between the cessation of normal rhythm and the establishment of an idioventricular rhythm. It is possible that in the case presented above a similar latent period affecting the auricles, with consequent cardiac arrest, occurred between the cessation of activity in the sinoauricular node (sinoauricular block) and the establishment of auricular fibrillation. Since a common interpretation is that the paroxysmal auricular arrhythmias are

due to auricular irritability, it may be that in some cases these arrhythmias represent an auricular escape as a result of a depressed sinoauricular node instead of the commoner ventricular escape. Depression of the sinoauricular node is usually functional and the result of vagal activity, although there is some evidence that in older patients the node may be depressed as a result of impaired circulation due to coronary-artery disease.

Of the two possible mechanisms discussed above, the former appears to rest on a sounder experimental foundation and seems the more probable. Both, however, are purely speculative so far as the present case is concerned.

CONCLUSIONS

Faintness and syncope associated with some cases of paroxysmal auricular fibrillation may not be due to a fall in blood pressure and cerebral ischemia as a result of a rapid ventricular rate but rather to asystole during a latent period between the cessation of normal rhythm and the establishment of the auricular arrhythmia. Either the cardiac standstill or the auricular fibrillation, or both, may be of vagotonic origin.

48 Penobscot Street

MEDICAL PROGRESS

PHYSIOLOGY*

HEBBEL E. HOFF, M.D.†

NEW HAVEN, CONNECTICUT

SURGICAL PHYSIOLOGY

NO SMALL part of medical progress arises from the attempt to express the changes taking place in disease in terms of the physical sciences and it is no longer necessary to defend the advantages of a scientific training as a basis for a career in medicine. One of the more interesting indications of the popularity of this trend is the appearance of books that purport to interpret to the practicing physician one of the basic sciences involved in his specialty. One remembers Hewlett's *Pathological Physiology of Internal Disease* as an earlier work of this kind. Peters and Van Slyke's *Quantitative Clinical Chemistry* is without question the model for all subsequent attempts,

and establishes criteria by which they must be judged.

The first essential of a book of this kind is that the material it presents and the statements it makes should, so far as possible, be correct, or should represent the result of a rational criticism of available data. Secondly, the applicability to man and to the specialty of the material presented should be most carefully scrutinized. Thirdly, the author should take pains to point out subjects in need of clarification, and should facilitate more extended study by careful documentation at every point. Finally, there is the requirement of completeness of coverage, not demanded in a monograph, but essential in a book of this type.

Judged by such rigorous standards, a recent volume, *Surgical Physiology*, by Nash¹ falls somewhat short of expectations. There seem to be no gross errors in fact, but a number of minor flaws can be seen, such as the statement (page 34) that

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. \$4.00).

*From the Laboratory of Physiology, Yale University School of Medicine.

†Associate professor of physiology, Yale University School of Medicine.

ordinary fainting attacks are "largely due to vagal slowing of the heart." An example of uncritical handling of material is the discussion (page 43) of plasma potassium in shock without reference to the physiologic effects of potassium, or the possible toxic effects of an elevation of plasma potassium. A typical example of failure to consider the applicability to man of physiologic data is the assertion (page 5) that "experimentally an excess of calcium ions causes standstill of the heart in extreme systole, a condition known as 'calcium rigor.'" This phenomenon occurs in the frog and turtle heart, but not in the mammalian heart, in which ventricular fibrillation or arrest without rigor may be the terminal event. The bibliography is limited, and not in a very useful form, and most statements are without documentation. Among the problems dealt with inadequately or not at all are the cardiovascular complications in anesthesia, the lymphatic system and the clotting of blood.

There is perhaps another way of judging this book. It does present material that is rather widely diffused in the literature, and thus serves as a compact and ready source of the salient points of many a subject.

A surgeon with ready access to a well kept library would probably be better satisfied to consult, first, Wigger's *Physiology in Health and Disease*, Best and Taylor's *The Physiological Basis of Medical Practice* or—what in my opinion is still better—Bard's *Physiology in Modern Medicine*, and then to continue the subject in a specialized monograph like Peters's *Body Water* or Salter's *The Endocrine Function of Iodine*. Finally, he could work through the specialized reviews in journals into the original articles. Surgeons not so fortunately situated will find Nash's volume of considerable assistance in reaching an understanding of the physiologic basis of their surgical problems.

ROLE OF VEINS IN SYNCOPE AND SHOCKLIKE STATES

Sudden collapse after what may have been a trifling injury, or following an unexpected fright, is a phenomenon commonly enough observed but surprisingly little understood. Lewis,² who described the condition in soldiers, termed it a "vaso-vagal collapse," being impressed by the slow pulse so frequently seen, and by the supposed value of atropine in its therapy. Later studies demonstrated that atropine did prevent the slowing of the pulse but did not influence the collapse, and Lewis pointed out that the vagus nerve was therefore not vitally concerned in the phenomenon, which presumably then implicated the vasomotor system. It is, of course, largely to the credit of Weiss³ that a collapse syndrome was defined in which the vagus nerve is basically responsible. Despite such

a clear separation of the two conditions, one continues to find references to the vagal origin of the so called "vasovagal syndrome," and to the necessity for atropine as a prophylactic or therapeutic measure.

The next major advance in the elucidation of the vasovagal syndrome, to which the term "primary shock" might also apply, was also made by Weiss.^{4,5} Although clinicians and physiologists described the phenomenon in vague terms of "vasomotor paralysis" or "splanchnic vasodilatation," Weiss was able to demonstrate that the locus of the circulatory disturbance is in the veins and venules, and possibly the capillaries, whereas the arterial tree shows, if anything, a vasoconstriction. In other words, the fall in blood pressure is due, not to generalized peripheral vasodilatation, which reduces the peripheral resistance to a degree where blood escapes from the arterial system so rapidly that a head of pressure cannot be maintained, but rather to the fact that the veins and venules dilate greatly and act as a reservoir for large amounts of blood. Venous pressure at the right auricle then falls, cardiac filling diminishes, and concomitantly, cardiac output and arterial blood pressure decrease. Later studies of a slightly different type (venous occlusion by ligature) indicate that the pooling of about a liter of blood is sufficient to induce symptoms of collapse.⁶

The experiments of Weiss involve the interaction of two factors: the upright posture on a tilting table, which reduces muscular activity in the dependent parts of the body, and the administration of small doses of sodium nitrite. Either procedure alone usually produces no symptoms, but the combination regularly induces the typical syndrome in which "the primary change consists in tachycardia, small arterial pulse pressure, with small pulse volume (thready pulse), fall in the venous pressure, and arteriolar vasoconstriction." Studying the cause of the fall in venous pressure, Weiss and his collaborators found that nitrites cause a profound diminution in the tone of the venous system, so that, to raise the venous pressure in a limb to a given level, far more blood would have to flow into the vessels of the part. The rate of inflow is diminished, indicating the presence of arteriolar vasoconstriction. In the absence of the muscular massage that normally promotes the emptying of veins toward the heart, such dilatable veins could not resist the force of gravity which tends to pool blood in dependent parts.

Inquiries emphasize the fact that therapeutic or prophylactic measures must be taken primarily to increase venous pressure. Restoration to the horizontal position is always rapidly effective. Larger doses of nitrites can cause collapse, even in the horizontal position, and elevation of the lower

part of the body is presumably an effective therapy. The common vasoconstrictor drugs—epinephrine and Pitressin—are without value, and Pitressin probably facilitates collapse.^{7, 8} Paredrinol (*a-n*-dimethyl-*p*-hydroxyphenethylamine) was shown to be distinctly useful in a number of cases, either preventing collapse completely or greatly delaying its onset.⁹ This substance, first studied by Rein,¹⁰ has a more active vasoconstrictor influence on the venous than the arterial portions of the circulatory system.^{12, 13}

Search is now being made for situations in which a similar loss of venous tone forms the basis for other shocklike phenomena. Paredrinol appears to be effective in severe cases of postural hypotension with syncope and is occasionally of value in the hypotension associated with acute infectious diseases. A decreased venous tone and the presence of postural syncope have been reported during the convalescent stages of such illnesses.¹³⁻¹⁵ Careful studies by Ebert and Stead,¹⁶ however, reveal that this is not the only, perhaps not the paramount, circulatory disturbance during the acute stage of infectious diseases, since elevation of the feet and intravenous infusions of whole blood, plasma or 10 per cent glucose fail to produce improvement in the circulation. The patients in whom these procedures were tried were virtually moribund, and in certain cases, elevation in blood pressure was evoked. It must also be recalled that Altschule and Gilligan¹⁷ and others¹⁸ have demonstrated how very quickly even large transfusions are compensated for by vasodilatation that includes arteriole and venuoles, so that only temporary changes in blood pressure are to be expected.

Denny-Brown and Russell¹⁹ offer evidence, which cannot be said to be completely convincing, that pooling in the venous system is responsible for the initial fall in blood pressure after concussion caused by blows on the head. They suggest "vasomotor paralysis" or stimulation of the glossopharyngeal-vagal mechanism as the responsible factor. These suggestions demonstrate how little is yet known of the pathologic physiology of the veins. From Franklin's²⁰ review of the data up to 1937, it appears that the veins of the abdomen are normally innervated by fibers of the sympathetic system; that section of these nerves dilates the veins, whereas stimulation of the peripheral stump of the nerve constricts them; that after ergotoxine to paralyze sympathetic hormonal effects, stimulation of the same nerve causes venous dilatation; and that the dilatation of the veins produced by tapping of the vein or the abdomen is a local effect not dependent on the central nervous system. At that time, Franklin could not find any circumstances in which reflex venous

dilatation had been demonstrated without question. The value of continuation of the studies inaugurated by Weiss is obvious.

RENAL BLOOD FLOW IN HUMAN HYPERTENSION

The method of Diodrast clearance, which Smith and his colleagues²¹ have shown to measure blood flow through the excretory portions of the kidney, has now been applied to a study of blood flow in human hypertension. These studies indicate clearly that a reduction in renal blood flow, which occurs in so-called "essential hypertension" may be of extreme degree.²²⁻²⁴ The administration of a pyrogenic substance (inulin), which causes an increase in renal blood flow in the normal kidney, has the same effect in the hypertensive kidney. Such findings are consistent with the view that in such kidneys, a reversible vasoconstriction exists, perhaps in the efferent vessels of the glomerulus. The same studies detect a variable decrease in the total excretory mass, denoting a destruction of kidney substance. In no case of essential hypertension was it possible to detect any difference between the degree of involvement of the two kidneys.²⁵ In a study of 5 patients with hypertension associated with unilateral renal damage, a marked difference in the blood flow in the two kidneys was detected, although the blood flow in the supposedly normal kidney was also below normal.²⁶ Removal of the diseased kidney was followed in all 5 cases by an increase in the blood flow in the remaining kidney. A significant fall in blood pressure took place in 3 of the 5 patients, but in none was a normal blood pressure re-established, although in 3 cases a normal blood flow was established in the remaining kidney.

An unexpected finding is that in the hypertension of toxemia of pregnancy, in the pretoxemic state, or in the hypertensive state following toxemia of pregnancy, no indication of diminution in renal blood flow can be demonstrated.²⁷⁻³⁰ Some evidence of increased blood flow is occasionally made out. These experiments cast certain grave doubts on any theory that explains all types of hypertension in man on the basis of renal ischemia. They do not, however, necessarily indicate that the hypothesis of a renal origin of hypertension need be abandoned. Corcoran and Page³¹ call attention to the fact that dogs showing hypertension in response to renal arterial obstruction may also give normal Diodrast clearances. The persistence of experimental renal hypertension in the absence of renal ischemia is consistent with their view that intrarenal reduction of pulse pressure, rather than ischemia, may be the effective cause of experimental renal hypertension. The renal origin of the hypertension of toxemias of

pregnancy therefore still remains a possibility. The diminished renal blood flow in essential hypertension, of course, is also consistent with the renal origin of the disease, but there remains the possibility that the reversible vasoconstriction observed is only the renal manifestation of the generalized vasoconstriction that maintains the hypertension.

INDUCTION OF VENTRICULAR FIBRILLATION

In man, ventricular fibrillation most frequently occurs as a sequel to an idioventricular tachysystolic episode. Several important factors in its origin have been pointed out, such as the facilitating influence of adrenalin or sympathetic stimulation in light chloroform anesthesia or acute benzol poisoning and that of intraventricular block in the fibrillation of heart disease. Recently, Wiggers and his co-workers³²⁻³⁵ have analyzed in some detail the fibrillation occurring after single intense electrical shocks, after a series of induction shocks, and after anodal and cathodal polarization. In all these circumstances, it appears that a sequence of ventricular extrasystoles is set up, comprising in fact a short run of ventricular tachycardia in which all beats originate from the same focus. These impulses are at first conducted radially away from the point of origin and involve the entire ventricular mass. Each successive beat arises after a slightly reduced interval, and is conducted away from its site of origin. After a very few beats, one wave is found to be traveling only a centimeter or two behind the previous beat. At this point, two alternative events may occur: the next beat meets refractory tissue in all directions and is blocked completely, or block is irregular, and some avenues are still open to it. In the latter event, the stage is set for the establishment of so called "circus motion," which constitutes ventricular fibrillation.

The intense single shock or the polarizing currents appear to create the initial series of tachysystoles by causing failure of the normal accommodation to internal or external stimuli, but obviously any tachysystoles may ultimately lead to ventricular fibrillation. Whether or not ventricular fibrillation develops must depend in the main on the state of the intracardiac conduction system. Any factors favoring the irregular development of intraventricular block must promote fibrillation, as Davis and Sprague³⁶ pointed out in 1928. Wiggers's theory seems to be essentially the same as that proposed by Nahum and Hoff³⁷ to account for the development of fibrillation by an intravenous injection of potassium chloride. These authors were impressed by the fact that fibrillation did not take place if marked reduction of cardiac rhyth-

micity occurred concomitantly with the development of intraventricular block, whereas fibrillation did occur if rhythmicity were maintained while block developed. They concluded that for the genesis of ventricular fibrillation two factors were essential: the presence of foci of automaticity in the ventricles, and intraventricular block. It is apparent that in the presence of an automatic focus of increasing rhythmicity, fibrillation may begin because of physiologic blocking in an otherwise normal heart. On the other hand, a heart in which damage to the myocardium has produced regions of varying block should be more susceptible to fibrillation than a normal heart. In a preliminary communication, Harris et al³⁸ have extended their observations to include the fibrillation following occlusion of a coronary artery, and find a similar mechanism operating.

COAGULATION OF BLOOD

The so called "classic theory" continues to retain validity as the basic explanation of blood coagulation. The reaction in two stages of prothrombin, calcium and thromboplastin to form thrombin, and of thrombin and fibrinogen to form fibrin, has been the subject of repeated examination. Although no insurmountable obstacle to its continued acceptance has as yet appeared, much has been learned of the nature and source of the individual factors, and of their role in the various hemorrhagic diseases. Excellent reviews by Quick³⁹ and Howell^{40, 41} deal particularly with this problem.

The role of vitamin K in the production of prothrombin is now well recognized and needs no further review. An equally promising field, now in the stage of active development, deals with the nature of the thromboplastic substance. The recent significant contributions in this field are largely those of Taylor and his co-workers.

These studies began with the observation of Patek and Taylor⁴² that from the blood plasma of normal human subjects there can be precipitated by dilution and acidification a globulin fraction that contains a clot promoting substance for hemophilic blood. The material is active while fresh, or after drying in a vacuum. The same treatment of hemophilic blood yielded a precipitate that had little or no clot-promoting ability. Tested in a calcium fibrinogen system, precipitates from both normal and hemophilic blood had equal prothrombin activity.

Later studies⁴³⁻⁴⁵ demonstrated that both prothrombin and fibrinogen could be removed from this globulin substance without impairing the clot-promoting faculty for hemophilic blood. Further fractionation then demonstrated that all this clot-

promoting activity could be found in a euglobulin fraction. From these studies and from those of Howell,^{40, 41} it becomes clear that the essential defect in hemophilia is the absence or deficiency of a euglobulin fraction of the plasma, which, in terms of the classic theory, may be designated as "plasma thromboplastin."

This observation immediately directs attention to the blood platelets. Quick³⁹ observes:

Thromboplastin is widely distributed in the body as an intracellular substance. In the blood it occurs locked up in the platelets and perhaps is present also in the leukocytes. Certain tissues, notably the brain, lungs, and thymus, are particularly rich in thromboplastin. It apparently never occurs free, but is liberated whenever tissue cells are injured or ruptured. *In blood uncontaminated by tissue juices, the thromboplastin is liberated solely by the platelets. The liberation of thromboplastin by the platelets, therefore, appears to be the prime factor in determining the clotting time of blood obtained by venipuncture.* [italics mine].

It is, of course, well known that no quantitative change in the platelets exists in hemophilia, and the reviews of the question of qualitative changes by Quick and Howell yield no very convincing evidence. It is equally recognized that great reduction in platelets may occur in thrombocytopenic purpura without change in the coagulation time of venipuncture blood. In view of these and other doubts cast on the platelet origin of plasma thromboplastin, Lozner and Taylor⁴⁶ have recently completed a most interesting study on the effect of foreign substance on blood coagulation.

The orientation of their work may be described most effectively by direct quotation:

It has been known for many years that the coagulation time of blood taken in paraffin tubes is much longer than that of blood taken in glass tubes. The explanation usually afforded is that the glass, acting as a foreign surface, destroys the platelets at a more rapid rate than occurs in the presence of paraffin. The increased amount of thromboplastin so liberated is then considered to be responsible for the shorter coagulation time in glass vessels. Nolf has criticized this explanation. He states that his experimental data indicate that cell- and platelet-free plasma already contains all the factors necessary for blood coagulation. He believes that the initiation of coagulation is the result of direct modification of one or more of the constituents of cell-free plasma by contact with a foreign surface such as glass.

Four types of experiments were carried out, normal human blood obtained by clean venipuncture being used. In the first series, normal human plasma was employed without the addition of anti-coagulants. The blood was drawn in an oiled syringe and transferred to a Lusteroid (a synthetic plastic) tube. Centrifugation at 4200 revolutions per minute for ten minutes gave a clear plasma with a platelet count of 8000 per cubic millimeter,

essentially "platelet free." The plasma was then transferred to tubes of different materials in collodion pipettes, and the coagulation times determined. This was 11 minutes in glass, 64 minutes in collodion, 44 minutes in paraffin, and 49 minutes in Lusteroid. Since the plasma was platelet free, it must be concluded that all the elements necessary for coagulation were present in the plasma at the time it was removed from the centrifuge, and that the accelerating effect of glass was not exerted on the platelets.

In the second series of experiments, blood was transferred into Lusteroid tubes containing citrate, and a platelet-rich plasma obtained by slow centrifugation. Samples were transferred to the four tubes and stored for an hour. No destruction of platelets was found in any of the tubes as determined by platelet counts at the beginning and end of the storage period. Nevertheless, when samples of the plasma were recalcified in Lusteroid, the plasma stored in glass showed a coagulation time of six minutes, whereas the coagulation times of the other plasmas were prolonged. When cell-free plasma was stored as described above and then recalcified in Lusteroid, the glass-stored plasma clotted in eleven minutes, whereas that stored in paraffin, collodion or Lusteroid clotted in from eleven to thirty-nine minutes. These experiments indicate that glass storage does not destroy platelets, but does bring about a change in citrated plasma, either platelet rich or platelet free, that promotes coagulation when calcium is added.

A third series of experiments demonstrated that storage in glass increases the clot-promoting activity of either cell-free or cell-rich plasma when added to hemophilic blood. Finally, it was found that the preparation of the globulin substance (Howell's plasma thromboplastin) in glass vessels yielded a product of far greater clot-promoting properties than that prepared in paraffin or collodion vessels.

The authors conclude:

The foregoing observations show that the effect of foreign surfaces on blood coagulation are [*sic*] essentially independent of the intact platelet. These studies indicate that the site of action of such surfaces is dependent upon a factor which is present in normal cell-free plasma, independent of prothrombin and fibrinogen associated with the euglobulin fraction of the protein and concerned with the clot-promoting activity of plasma for hemophilic blood [that is, plasma thromboplastin, according to Howell's nomenclature]. That this globulin substance might be derived from damaged platelets cannot be excluded by the present observations. However, it is present in cell-free plasma, and foreign surfaces have entirely similar effects, on platelet-free and platelet-rich plasma. The data presented clearly indicate that the effect of foreign surfaces is not accompanied by an increased lysis of the platelets prior to clot formation as heretofore assumed.

Taylor and Lozner tentatively offer Gortner and Briggs's⁴⁷ suggestion that glass activates thromboplastin by virtue of its surface electrical charge.

This evidence that all the necessary factors for clot formation are found in normal circulating plasma raises new and interesting problems. It seems to afford an explanation for the presence in circulating rabbit plasma of a clot-promoting factor observed by Parfentjev⁴⁸ and demonstrated by Taylor et al.^{49, 50} to be a true thrombin. It is possible that, in the rabbit at least, the reaction of prothrombin, calcium and plasma thromboplastin is a continuous one, and that small quantities of thrombin are constantly being formed. Why this thrombin does not react with fibrinogen to form fibrin remains a question, but its presence without clot formation indicates the presence of an anticoagulant. One should recall both the observation of Lozner, Joliffe and Taylor⁵¹ of a patient with a hemorrhagic diathesis, with prolonged clotting time associated with a circulating anticoagulant, and Quick's³⁹ belief that heparin is normally present, in combination with albumin, in circulating blood, where it exerts an anti-thrombin effect.

NEUROMUSCULAR TRANSMISSION

The recent work of Nachmansohn et al.^{52, 58} has introduced a decidedly new point of view into a subject that at times seemed to have degenerated into a controversy between proponents of the so-called "electrical" and "chemical" theories of neuromuscular transmission. These studies have in great measure concerned the discharge of the electric organs of certain fish,—notably, the torpedo, the ray and the electric eel,—in which the electric organ is composed essentially of modified muscular end plates arranged in series, all other muscular elements having disappeared in the evolution of the structure. In these organs, discharge caused by stimulation of the appropriate motor nerve is accompanied by the liberation of acetylcholine. The injection of acetylcholine produces an electrical discharge, and the previous injection of eserine increases and prolongs the discharge produced by nerve stimulation or by acetylcholine. Nachmansohn and his associates have also demonstrated the presence of a high concentration of acetylcholine esterase in the electric organ, a concentration that varies directly with the intensity of the electrical discharge.

Considering these facts together with the observations that acetylcholine esterase is present in all nervous tissue and that it is concentrated at the surface of the tissue rather than in the axoplasm, the authors come to the following conclusions:

acetylcholine participates in nerve transmission in all parts of the nervous system, and is not specifically limited to junctional tissues such as the synapse and the neuromuscular junction; and, in some fashion, the liberation of acetylcholine is responsible for the development of the electrical discharge that characterizes the physiologic activity of all nervous tissue and is recognized as a surface phenomenon.

In addition, these studies reveal the concentration at the surface of the axon of a high concentration of vitamin B₁, and suggest that this hormone is also implicated in the metabolism of acetylcholine. The hormone is essential for the metabolism of pyruvate, one stage of which yields acetate, and in the absence of vitamin B₁, the acetylation of choline to form acetylcholine is deficient. These observations therefore suggest that one of the essential biochemical lesions in the polyneuritis of vitamin B₁ deficiency is a diminished formation of acetylcholine and a consequent failure of nerve transmission.

A satisfactory schema of neuromuscular transmission can be constructed if, in addition to the above, the recent studies of Eccles and his co-workers^{59, 63} are considered. These investigators have for a number of years studied the electrical events occurring at the neuromuscular junction and have succeeded in recording potentials that appear to be derived from the motor end plate itself. They have shown that curarization diminishes the intensity of this potential, and that when the intensity decreases to less than 30 per cent of its normal value, failure of transmission occurs. End plate potentials show a slow decay, which permits summation of two successive potentials. If their combined height reaches 30 per cent or more of normal height, an impulse is set up in the muscle. Eserine antagonizes the action of curare by increasing the height of the end-plate potential.

There is therefore justification for the following theory of neuromuscular transmission: the impulse arriving at the end plate from the nerve liberates acetylcholine; the acetylcholine produces the end plate potential; and the end plate potential excites the muscle. There is no reason why a similar mechanism may not operate in transmission in the simple nerve fiber, with a repeated sequence of acetylcholine liberation, action current and excitation of adjacent tissue. The well known effects of action currents in stimulating surrounding tissue can be recalled. Recent studies of the effect of axon on axon⁶⁴ and muscle on its motor fiber⁶⁵ deserve attention.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28291*

PRESENTATION OF CASE

An eleven-year-old schoolgirl was admitted to the hospital because of pain "like a hammer blow" in the left flank, lower abdomen and thigh.

She had been in good health until nine months before entry, when there was a gradual onset of



FIGURE 1.

attacks of sharp, stabbing pain, beginning in the left costovertebral angle and radiating both to the groin and anterolateral surface of the left thigh as far as the knee and to the left lower quadrant of the abdomen. These attacks were aggravated by straining, coughing, sneezing and other sudden motions. They usually appeared in the afternoon, occasionally at night, when the patient lay in bed, and lasted up to an hour. They tended to increase in severity and in frequency. Aspirin af-

forded slight relief. There was no history of significant trauma.

On examination the patient appeared well developed. The chest and abdomen were normal. There was right lumbar scoliosis, and some spinal rigidity, with tenderness to the left of the second lumbar vertebra. All reflexes were intact, and there were no sensory disturbances. Naffziger's¹ test caused pain to radiate around into the left lower quadrant and down the anterolateral aspect of the thigh to the knee.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,420,000 with 13.2 gm. hemoglobin, and a white-cell count of 9800 with 60 per cent polymorphonuclears. The blood Hinton reaction was negative. The urine was normal. A lumbar puncture gave clear fluid under an initial pressure equivalent to 100 mm. of water. Bilateral jugular compression caused a rise in pressure to 250 mm. in thirty seconds, with a fall to 160 mm. in one minute after release; there were normal oscillations with the respiratory cycles. The total protein of the spinal fluid was 34 mg. per 100 cc., and the gold-sol curve was 0011100000.

A roentgenogram of the spine showed marked curvature of the lower dorsal and lumbar vertebrae toward the right. The individual bones and joints appeared normal, except for a large, sharply defined defect in the pedicle of the second lumbar vertebra on the left (Fig. 1). The uninvolved anterior portion of the pedicle was increased in density.

On the seventh hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. MARIUS N. SMITH-PETERSEN: I do not know what a pain like a "hammer blow" refers to, or whether that was the onset of pain or not. If it were the onset of pain, it might be significant; if it were persistent pain of a throbbing character, it might also be important—this statement is not clear. The hammer-blow pain might have been caused by a fracture superimposed on underlying disease.

Later in the history, we have a statement to the effect that the onset of pain was gradual and that the pain was sharp and stabbing in character. From this statement we can conclude that the hammer-blow pain probably did not refer to a fracture, superimposed on disease.

The distribution of pain was extensive: local pain in the left costovertebral angle, accompanied by radiation pain to the groin and to the anterolateral surface of the left thigh, as far as the

*The cases published in the July 16 issue of the *Journal* were incorrectly numbered "28301" and "28302," instead of "28291" and "28292." To keep the correct total, this and the following case have been given the numbers of those omitted.

knee; and radiation pain in the left lower quadrant of the abdomen. The radiation pain described is consistent with a lesion involving the twelfth dorsal and the first and second, possibly the third, lumbar vertebrae. From the subjective pain, then, we can localize the lesion at the dorso-lumbar junction.

"The attacks were aggravated by straining, coughing, sneezing and other sudden motions." This is worth noting since the pain arising from a lesion impinging on the spinal canal would be aggravated by straining, coughing and sneezing.

"They [the attacks] usually appeared in the afternoon, occasionally at night, when the patient lay in bed, and lasted up to an hour." Freedom from pain in the morning can be explained on the basis that the patient got up rested and carried herself better than she did later on in the day when she became tired. The lateral curvature could have been aggravated, and secondary strain thrown on the site of the lesion. The pain could not have been extremely severe or could not have increased very much, because the patient was not brought to the hospital for nine months after the onset.

"There was no history of significant trauma." We have no right to suspect the presence of a fracture unless it were superimposed on an underlying diseased condition.

"All reflexes were intact, and there were no sensory disturbances." These findings point away from a lesion involving the spinal canal.

Naffziger's test aggravated the pain radiating to the left lower quadrant and to the thigh. In my opinion, this reaction does not help us in making a differential diagnosis.

The blood picture, including the white-cell and differential counts, is against an infection, such as osteomyelitis.

A lumbar puncture was done. The dynamics were normal, but the total protein (34 mg. per 100 cc.) was high for a child of 11, pointing to possible irritation of the meninges.

X-ray films showed a sharply defined lesion in the pedicle of the second lumbar vertebra on the left. The uninvolved anterior portion of the pedicle showed an apparent increase in density. The appearance is consistent with a cyst and with xanthoma. Giant-cell tumor should be mentioned, but the patient is too young and I have never seen a giant-cell lesion in this location. Tuberculosis must also be mentioned, but I have never seen tuberculosis involving the pedicle. Hemangioma is my final alternative, but, again, I have never seen one in this region. Personally, I favor a diagnosis of cyst or of xanthoma.

DR. LAURENCE L. ROBBINS: I think I have seen this case before, so that it is not quite fair for me to

interpret the films. I should say that the important diagnostic point, so far as the radiologist is concerned, is the area of rarefaction with a rather sharp line of increased density around a portion of the margin. There is increased density in the pedicle, as described. I should not consider tuberculosis, and I do not believe that it is a hemangioma, because the usual appearance of hemangioma of the vertebra is more that of coarse striations.

DR. SMITH-PETERSEN: What would be your best guess?

DR. ROBBINS: I know the diagnosis, having seen the films before.

DR. TRACY B. MALLORY: I think it is fair to say, however, that the X-ray Department did not suggest the correct diagnosis preoperatively.

Would anyone care to make any other suggestion?

DR. ERNEST M. DALAND: How do you rule out Ewing's tumor?

DR. SMITH-PETERSEN: I cannot rule it out.

A PHYSICIAN: Is the scoliosis presumably entirely secondary?

DR. SMITH-PETERSEN: I think so. One cannot depend on the parents' observation. Time and again, one observes extreme scoliosis, just discovered. In this case, I think it is fair to say that it came on in response to pain.

DR. CHANNING C. SIMMONS: You have said that a giant-cell tumor is rarely seen at that age. I have been thinking it over, and I can think of 4 patients who were roughly under fourteen. If you were to ask me for the exact ages, I could not give them.

DR. SMITH-PETERSEN: I had a patient at the age of twelve who, according to the pathologists, had a giant-cell tumor; as time went on, the diagnosis was changed to cyst.

DR. FULLER ALBRIGHT: One sees giant-cell tumors in children with hyperparathyroidism.

CLINICAL DIAGNOSIS

Extradural tumor, at level of second lumbar vertebra.

DR. SMITH-PETERSEN'S DIAGNOSIS

Cyst, involving pedicle of second lumbar vertebra.

ANATOMICAL DIAGNOSIS

Osteoid osteoma of second lumbar vertebra.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was operated on by Dr. W. J. Mixter. The only preoperative diagnosis recorded is "tumor of the spine." They did

not commit themselves any closer. An evident tumor mass, consisting of obviously abnormal, rather soft bone, was found in the lamina of the second lumbar vertebra, and that, together with the transverse process, which was slightly involved, was removed. Microscopic examination showed a focus of intertwined osteoid trabeculae separated from each other by narrow bands of relatively acellular fibrous tissue. At the periphery of the lesion, the cortical bone was denser than normal. The picture is very characteristic of what Jaffe and Lichtenstein² have described as osteoid osteoma.

DR. SMITH-PETERSEN: As a matter of fact, Dr. C. B. Larson made that diagnosis. I talked this case over with him, and he suggested "osteoid osteoma."

DR. LARSON: It is unusual to find a punched-out lesion without more sclerosis of the bone around it.

DR. JACOB LERMAN: Did it involve the spinal canal?

DR. MALLORY: The operative note does not make that clear.

DR. SMITH-PETERSEN: It must have infringed on the spinal canal.

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CASE 28292

PRESENTATION OF CASE

First admission. A forty-nine-year-old white widowed painter was admitted complaining of inability to see to either side.

The patient was well until one year before admission, at which time he developed colicky pains in his abdomen, with nausea and vomiting in the morning. At the same time, he had gripping pains in both legs. There was also a feeling of weakness and lassitude. Some teeth were extracted, and a "lead line" of the gums was noted. Following this, he improved, although he continued to feel weak. Ten months before admission a physician examined his eyes; although the patient had no complaints, he was advised to wear glasses. The visual fields were normal. Three months prior to entry he noticed dimness in the left visual field of his left eye. This gradually increased. Three weeks before entry, it was thought that his left frontal sinus was at fault, and it was operated on. Immediately following the operation, the patient noted that he could not see well to the right side with his right eye. A few days after this,

his nausea and vomiting recurred. He had had rare headaches, but these had not increased during the last two years.

The patient had been a painter for eighteen years. One brother had diabetes. Seventeen years before entry, the patient had been kicked on the forehead by a horse, and five stitches had been taken; he had had no residual symptoms.

Physical examination showed a well-developed and well-nourished man in no distress. All but two lower teeth were missing. There was a slight postnasal discharge. Examination of the chest was negative. The remainder of the general physical examination was negative. Neurologic examination showed normal mentality. The fundi were normal except for slightly dilated vessels. The visual fields showed bitemporal hemianopsia. External ocular movements were normal, and there was no nystagmus. The pupils reacted normally to light and accommodation. The remaining cranial nerves were negative. The reflexes were normal and equal on both sides. There were no other neurologic abnormalities.

The blood pressure was 155 systolic, 100 diastolic. The temperature was 97.4°F., the pulse 80, and the respirations 20.

The urine showed a specific gravity of 1.012 on one occasion and 1.008 on another, but was otherwise normal. The blood showed a red-cell count of 4,200,000 with 60 per cent hemoglobin, and a white-cell count of 6800 with 72 per cent polymorphonuclears. A lumbar puncture showed an initial pressure of 175 mm. of water, which rose to 350 mm. with jugular compression on either side and fell normally to 180 mm. After withdrawal of 10 cc. of fluid, the pressure was 120 mm. The fluid contained 1 lymphocyte per cubic millimeter and 49 mg. of protein and 70 mg. of sugar per 100 cc. The gold-sol curve was 0011100000. The spinal-fluid Wassermann reaction was negative. A blood Hinton reaction was negative.

X-ray films of the skull showed no evidence of increased intracranial pressure. The pineal body was not definitely calcified. The sella turcica was quite abnormal in size and shape: it was greatly enlarged; the posterior clinoid processes were displaced backward, and the one on the right showed evidence of erosion and decalcification; and the right floor of the sella showed evidence of erosion. There was increase in the size of the lower jaw, and all the bones of the skull appeared slightly thicker and denser than normal. The hands showed increased length of all the bones and slight tufting of the terminal phalanges. The bones of the feet were abnormally large.

A course of deep x-ray therapy was given over the pituitary gland: 800 r to the left sella, 800 r to

the right, and 600r to both the anterior and posterior portions of the skull. After the third treatment, the patient was subjectively much improved and noticed a clearing of his visual fields. After his full course of therapy, however, visual-field determinations showed that there were still bilateral defects. On the thirty-first hospital day, an operation was performed. Between the optic nerves, which were definitely separated, was a bulging, blue-gray tumor, evidently arising in the pituitary fossa. It was explored with a needle, and about 5 cc. of brown fluid removed. The capsule was then incised, and a considerable amount of tumor curetted out. The sac seemed to be completely emptied but could not be removed because of the presence of large vessels. Pathological examination of this specimen revealed dense connective tissue containing large thin-walled vascular channels, but no epithelium. The patient improved rapidly following the operation and was discharged on the forty-ninth hospital day, with instructions to return after two weeks for visual-field examinations.

Second admission (six years later). The patient was not re-examined until one year after he was discharged, at which time visual fields showed moderate generalized narrowing on both sides. He had had no complaints until two years before his second admission, when he began to see dark spots in front of his eyes, associated with dyspnea, at the same time feeling as though he would drop. Six months before admission, he was unable to sleep well. Two months later, he had an attack of "flu," characterized by weakness, malaise and fever, and remained in bed for three weeks. Following this, he was weak and fatigued; his speech became slow, and anorexia severe. Intermittent nausea and vomiting recurred. There was no evidence of blood in the vomitus, and the vomiting was not projectile in type; it usually occurred immediately after a meal. The patient had had no headaches or convulsions. During the previous three months, he had noticed an increased sensibility to cold weather and generalized muscle aches. Two months before entry, visual-field determinations in the Eye Clinic showed marked narrowing on all sides, especially in the upper temporal fields. The visual acuity was 20/20 in the right eye, and 20/30 in the left. The fundi showed slight atrophy of the nasal side of each disk. Six weeks before admission, the patient entered the Thyroid Clinic, where a basal metabolic rate of -21 per cent was found. His skin was dry, and there was slight myxedema of the neck and face. A slowing of his mental processes was noted. Thyroid therapy was begun. During the previous two

years, his weight had dropped from 210 to 175 pounds.

Physical examination on entry showed a slightly obese, well-developed and well-nourished man in no distress. The skin was pale and soft, but not dry or brittle. The hair was soft and silky, and the hair over the body was decreased in amount. The face was puffy. Examination of the fundi was essentially negative. The visual acuity was 20/20 in each eye. The visual fields showed only slight bitemporal narrowing, more marked on the right. The tongue deviated slightly to the right. Examination of the chest was negative. The abdomen was normal. There were no other pertinent findings.

The blood pressure was 140 systolic, 88 diastolic, lying down; 138 systolic, 92 diastolic, sitting; and 118 systolic, 92 diastolic, standing. The temperature was 98.6°F., the pulse 72, and the respirations 20.

Urine examination showed a specific gravity of 1.018; there were no abnormal findings. The blood showed a red-cell count of 4,100,000 with 65 per cent hemoglobin, and a white-cell count of 8000 with 41 per cent polymorphonuclears, 11 per cent large lymphocytes, 27 per cent small lymphocytes, 10 per cent mononuclears, 7 per cent eosinophils, 2 per cent basophils and 2 per cent unidentified cells. The smear showed slight achromia. The nonprotein nitrogen of the serum was 27 mg. per 100 cc., the chlorides 96 milliequiv. and the sodium 130 milliequiv. per liter, and the cholesterol 170 mg. per 100 cc. A sugar-tolerance test showed 87 mg. per 100 cc., fasting; 121 mg., in half an hour; 84 mg., in one hour; 98 mg., in two hours; and 112 mg., in three and a half hours. A blood Hinton reaction was negative. The basal metabolic rate was -22 per cent. A stool examination was guaiac negative. An electrocardiogram showed rather low voltage of the QRS complexes and T waves.

X-ray films of the skull showed marked enlargement of the sella, with marked decalcification of the dorsum sellae and posterior clinoid processes. There was no evidence of increased intracranial pressure. Films of the hands showed that all the bones were rather heavy; there was questionable tufting of the terminal phalanx of the fourth right finger. The chest films showed multiple areas of calcification scattered throughout both lung fields, particularly marked in both apical fields. The heart was normal.

The patient was given a high-salt diet and salt in gelatin capsules. Progressive improvement was obvious subjectively and objectively, and within twenty-four hours, his weakness and malaise had diminished considerably. He was discharged on the thirty-second hospital day.

Final admission (nine months later). The patient was seen one month after discharge, at which time his improvement had continued. A serum sodium at that time was 131 milliequiv. per liter, a potassium 3.8 milliequiv. and a total fixed base 139 milliequiv. Four months before re-entry, he developed general malaise, weakness, lassitude and aching in the joints. Following this, he had occasional fainting spells preceded by a feeling of increased weakness and perspiration. Many of these impending attacks were warded off by absolute rest and sugar by mouth. Two weeks before admission, on closing his right eye, he noticed that the temporal half of his left visual field was blind. He had no other complaints. He had gained 10 pounds in weight during the previous four months.

Physical examination showed a well-developed and well-nourished man in no distress. The skin was dry, pale, parchmentlike and cold. The hair of the scalp and pubic regions was rather scanty. There was no bulging about the craniotomy scar. Examination of the chest was negative. The abdomen was normal. The fingers were enlarged. The testicles were somewhat smaller than normal. Neurologic examination showed that the patient was intelligent and co-operative. His speech was slow. The pupils were equal and active. External ocular movements were full, without nystagmus. The fundi were normal. Visual-field determinations showed a left temporal hemianopsia and dimness in the right temporal field. Visual acuity was 20/20 in the right eye, and 20/50 in the left. The remaining cranial nerves were normal. Motor and sensory examinations were negative except for slight impairment of the vibratory sense over the left foot and ankle.

The blood pressure was 150 systolic, 105 diastolic. The temperature was 98.6°F., the pulse 70, and the respirations 20.

Examination of the urine was negative. The blood showed a red-cell count of 4,850,000 with 75 per cent hemoglobin, and a white-cell count of 6100 with 45 per cent polymorphonuclears, 50 per cent lymphocytes, 2 per cent mononuclears and 3 per cent eosinophils. A blood Hinnin reaction was negative. The fasting blood cholesterol was 180 mg. per 100 cc. The serum sodium was 132 milliequiv. per liter, and the total fixed base 141 milliequiv. A lumbar puncture showed normal pressure and normal dynamics. The fluid was clear and contained only 2 lymphocytes per cubic millimeter. The total protein was 93 mg. per 100 cc., and the sugar 59 mg.; the gold-sol curve was 0001110000.

X-ray films of the chest showed no change since the previous examination. Those of the skull were essentially the same.

On the twentieth hospital day, an insulin-tolerance test was done following a dose of 6 units of insulin; the blood-sugar levels at twenty, thirty, forty-five, sixty, ninety and one hundred and twenty minutes were 81, 58, 62, 68, 83 and 93 mg. per 100 cc., respectively. The corresponding blood pressures were as follows: 150 systolic, 100 diastolic; 130 systolic, 90 diastolic; 104 systolic, 70 diastolic; 110 systolic, 76 diastolic; 120 systolic, 80 diastolic; 136 systolic, 30 diastolic; and 136 systolic, 98 diastolic. A course of x-ray therapy was given, which included 1200 r to each of four portals. Following this, the patient's condition was essentially unchanged. On the thirty-fifth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD C. REIFENSTEIN, JR.: This is a very interesting case history. Let us retrace the involved course of events from the time that the patient became ill one year before his first admission to the hospital, which was about seven years before his second operation.

The first episode described in the history was an acute attack of abdominal colic, nausea, vomiting, gripping pains in the legs, weakness and lassitude. Such symptoms in a man who has been a painter for eighteen years and who is found to have a lead line of the gums indicate an acute attack of lead poisoning. The pains in the legs were probably manifestations of peripheral neuritis, which is not uncommonly seen in plumbism. It is interesting that the patient recovered from this neuritis without exhibiting a paralysis of the most used muscles of the legs, which is frequently encountered in acute intoxication with lead. It seems to me most unlikely that the lead poisoning had anything to do with the events that followed.

Nine months later the patient developed his next symptom: dimness in the left visual field of the left eye. The first thought that occurs to one is that the eye symptoms were related to the attack of lead poisoning and, hence, that the patient was developing an optic neuritis. The recurrence of nausea and vomiting shortly afterward also calls to mind the nausea and vomiting that were present during the attack of plumbism. However, nausea and vomiting do not usually present themselves as symptoms of plumbism in the absence of colic. Although it has been observed frequently that patients who have a considerable deposit of lead in their bones are apt to develop symptoms of acute intoxication with lead during a severe or protracted illness, in the present case, the patient, at the time of the recurrence of the nausea and vomiting, did not seem to have been sufficiently ill to have induced such a recurrence of

plumbism. Furthermore, the lack of other manifestations of lead poisoning and, particularly, peripheral neuritis at this time makes this interpretation doubtful. The demonstration of normal optic disks and bitemporal hemianopsia and the infrequency of the headaches help us to eliminate the question of lead intoxication from further consideration.

The finding of bitemporal hemianopsia immediately suggests an intracranial lesion, which provides a more likely explanation for the occurrence of nausea and vomiting. The slightly dilated retinal vessels, the slightly increased cerebrospinal-fluid pressure, the slightly increased cerebrospinal-fluid protein in the absence of cells, and the weak Type II gold-sol reaction are consistent with this interpretation. Furthermore, the bitemporal hemianopsia serves to localize the lesion as impinging on the optic chiasm. The x-ray evidence of a greatly enlarged sella turcica, with backward displacement of the posterior clinoid processes and erosion of the one on the right and the right floor of the sella, makes the picture complete. The clinical diagnosis of an intracranial lesion in the region of the pituitary gland warranted a trial of x-radiation therapy. When this proved ineffective, operation was indicated in an effort to protect the eyesight. The demonstration of the tumor mass at operation supplied the final proof of the correctness of the clinical diagnosis.

The major diagnostic problem in this case is the nature of the tumor mass that was found at operation. Before considering this, however, let us follow the subsequent course of the patient. For four years after the first operation, the patient was relatively free from symptoms. It is therefore reasonable to assume that the tumor mass, which seemed to be arising in the pituitary fossa, had not, up to that time, destroyed enough of the pituitary gland to interfere seriously with its function.

Two years before the second operation (four years after the first operation), however, a new sequence of events appeared. Not only did the visual symptoms become worse, suggesting that the tumor mass was again causing pressure on the optic chiasm, but, in addition, the patient developed increasing signs of insufficient function of the anterior pituitary gland. From a clinical point of view, the patient began to exhibit a considerable degree of so-called "panhypopituitarism"—that is, underfunction of all the elements of the anterior pituitary gland. There was evidence of inadequate function of the adrenal cortex: weakness, malaise and fatigue; Addisonian crises, with anorexia, nausea and vomiting; a loss of 35 pounds of weight; slight fall in blood pressure (from 155 systolic, 100 diastolic, on the first admission to 140

systolic, 88 diastolic); low serum sodium, chloride and total base values; and clinical improvement with a high-salt intake. There was also evidence of underfunction of the thyroid gland: increased sensibility to cold; dry, pale and soft skin; myxedema of the face and the neck; poor myocardial tone; generalized muscular aches; slowness of the mental processes; and a diminished metabolic rate. The fact that the basal metabolic rate on the second admission to the hospital was still -22 per cent in spite of thyroid therapy, which had been started six weeks before (and presumably was continued), suggests that the patient was not suffering from true myxedema (which would have responded by then), but rather from hypofunction of the thyroid gland secondary to underfunction of the anterior pituitary gland (which often fails to respond adequately to the usual thyroid therapy).¹ There was some evidence, furthermore, that the gonads were underfunctioning: a decrease in the amount of body hair; and testes somewhat smaller than normal. The glucose-tolerance test revealed increased tolerance: that is, the patient was hyperglycemia resistant. This finding is consistent with panhypopituitarism.² In spite of a high-salt intake and thyroid therapy, the patient began to have attacks of faintness associated with increased weakness and perspiration. These attacks were probably hypoglycemic attacks, since patients with panhypopituitarism are subject to such episodes, and since the attacks were controlled by the ingestion of sugar. There is no definite statement in the history that the patient was still receiving thyroid medication, but if so, this therapy may have induced the hypoglycemic attacks. We have seen several similar patients in whom this occurred. Thyroid medication also frequently induces Addisonian crises in these patients.

All these data make a strong case for the existence of a state of panhypopituitarism during this period. The one disturbing feature is the result of the insulin-tolerance test, which was normal. One would expect in panhypopituitarism to have hypoglycemia unresponsiveness—that is, inability to raise the blood-sugar level after an insulin-induced hypoglycemia. Furthermore, a full dose of insulin (0.1 unit per kilogram of ideal body weight) was given without any reaction, whereas patients with panhypopituitarism are so sensitive to an insulin-induced hypoglycemia that it is customary to give only a half to a third of the calculated dose of insulin to avoid reactions. In thus attaching significance to the insulin-tolerance test, we are assuming that the patient was properly prepared for the test by being placed on a diet containing at least 300 gm. of carbohydrate for at least three days prior to the test, and that he was

fasting for exactly twelve hours before the test was begun. If these conditions were not observed, the results of the test must be discarded.

It is unfortunate that we do not have available the results of 17-ketosteroid assays in this patient. This test measures the excretory products of the adrenal glands and the testes.³ In panhypopituitarism, the levels are almost invariably less than 0.5 mg. of steroid per twenty-four hours—that is, for practical purposes, negative. If we accept as valid the results of the insulin tolerance test, we must assume that some normal anterior pituitary gland tissue was still present and, therefore, that the 17-ketosteroids would not be negative, although they undoubtedly would be low, perhaps about 2 to 3 mg. per twenty four hours.

The increase in visual disturbance with atrophy of the nasal side of each disk, along with the gradual onset of some degree of pituitary underfunction, indicates that the tumor mass was again causing pressure on the optic chiasm. This is substantiated by the definite increase in the spinal fluid protein level. Since x-ray therapy was again ineffective, the only recourse was to attempt to remove the tumor surgically, in the hope of saving the eyesight.

Let us now consider what lesions may cause pressure on the optic chiasm. In order of frequency are found an adenoma of the pituitary gland, a so-called "suprasellar cyst" or craniopharyngioma and, finally, a lesion such as a glioma of the chiasm, a meningioma arising from the floor of the third ventricle, a tumor such as a chordoma or a cholesteatoma, or even a chronic circumscribed arachnoiditis. The chiasm is also occasionally compressed from one or both sides by an aneurysm or varicose dilatation of one or both carotid arteries. However, since bitemporal hemianopsia was present in the case under discussion, and since this disturbance rarely occurs except with pituitary adenomas or suprasellar cysts, we can limit our discussion to these two types of lesions.

There are three types of anterior pituitary adenomas: the eosinophil (acidophil), the chromophobe and the basophil, corresponding to the three types of cells found in the gland. The basophil adenomas are extremely rare, and never attain an appreciable size; therefore, in view of the x-ray evidence of a large lesion and the findings at the first operation we can eliminate this type of adenoma from further consideration.

Eosinophil adenoma is a tumor of hormone-producing cells and it is thus accompanied by evidence of increased production of these hormones. These hormones would produce acromegaly in a man of forty-nine. Are there any evidences of acromegaly in the patient under discussion? There is no history of an increase in the size of the jaw,

head, hands or feet. In x-ray films of the jaw and skull, the bones were interpreted as thicker and denser than normal, also the bones of the hands and feet were stated to be increased in length or "abnormally large." But large or long bones do not necessarily mean acromegaly unless there is a history of a recent increase in the size of these bones. The increased density of the bones can be explained just as well as the result of the chronic deposition of small amounts of lead in the bones over a period of eighteen years. At one time, it was thought that tufting of the terminal phalanges was diagnostic of acromegaly, we have since found this manifestation in many other conditions and now attach no particular significance to it. One of the findings on x-ray study that is of great help in diagnosing acromegaly is an increase in the anterior dimensions of the bodies of vertebrae, particularly the thoracic vertebrae. This is seen best in lateral films taken over the thoracolumbar spine. Unfortunately this film was not taken. As a result of this change, the patient is not able to bend over and touch his feet. This disability is not mentioned in the physical examination of our patient, and therefore may be assumed to be absent.

Another test of considerable diagnostic aid in acromegaly also was not done—the level of the phosphorus in the blood serum. Since patients with acromegaly are growing, the phosphorus level is almost always significantly elevated (4 to 6 mg. per 100 cc.) compared with the normal adult levels (about 3 to 4 mg.)⁴ In fact, the level in acromegaly approaches that of a growing child.

Although the finding of hyperglycemia resistance is characteristic of panhypopituitarism, it may occur in acromegaly during the stage of so-called "compensatory hyperinsulinism." As a matter of fact, there is considerable variation in the type of curves obtained in the glucose tolerance, the glucose and insulin tolerance and the insulin tolerance tests in acromegaly, and the sugar curves are thus of no aid in the diagnosis of the condition.²

In view of the lack of history of an increase in size of the acral parts, and the absence of the x-ray films of the spine and of serum phosphorus values, all of which are commonly employed as diagnostic tests by the endocrine consultants of the Massachusetts General Hospital, we must conclude that acromegaly was not seriously considered by the physicians in charge of this patient during his stay in the hospital. Since all the reported x-ray findings are capable of another interpretation than acromegaly, I believe that this patient did not have an eosinophil adenoma. Furthermore, eosinophil adenomas are said to be sensitive to x-radiation, and the lack of response in our patient to two different courses of radiation is additional evidence

against this diagnosis. However, in dismissing an eosinophil adenoma, it must be pointed out that chromophobe adenomas have been reported that have had a small number of eosinophil cells in them.

Final pathological diagnosis, therefore, rests between a chromophobe adenoma of the anterior pituitary gland and a craniopharyngioma. This is a very difficult decision clinically, since either of these lesions could produce a picture in every way comparable to that of the patient under discussion. Neither of these lesions is hormone producing, so far as we know. The differentiation between them is at times of more than academic interest, particularly in early lesions, since it is occasionally possible to remove completely the craniopharyngioma and, thus, to cure the patient. Usually, however, all the cyst cannot be removed, and the danger of recurrence then exists. Successful complete removal of a chromophobe adenoma is very rare, and even in cases in which the tumor was presumably completely removed, the danger of recurrence is always present. In the patient under discussion, complete removal of the lesion was not possible; hence the differentiation between the two lesions is only of academic interest. As is apparent from the preceding discussion, recurrence of the lesion is of no help in the differential diagnosis.

The age of the patient at the time of the appearance of the tumor symptoms favors the diagnosis of chromophobe adenoma, which occurs oftenest in the third to fifth decade, and rarely before fifteen years. Although craniopharyngiomas are congenital tumors and may occur at any age, more than half of them appear in childhood, and the rate of frequency is much diminished in persons older than twenty years. The history of trauma to the head suggests a suprasellar cyst; however, the fact that the tumor did not become active until sixteen years after the accident makes this relation rather dubious.

From a statistical point of view, a chromophobe adenoma is about three times more likely than a craniopharyngioma. Of 2023 cases of intracranial tumors compiled by Cushing,⁵ pituitary adenomas comprise about 18 per cent and congenital tumors about 6 per cent.

The x-ray findings on the whole, favor a craniopharyngioma. A chromophobe adenoma of the pituitary gland typically causes great ballooning of the sella turcica, and only about a third of the cases exhibit erosion of the bony framework of the sella. Irregular erosion of the clinoid processes and the dorsum sellae is the usual finding in craniopharyngioma. In the patient in question, great enlargement of the sella was present, which favors a chromophobe tumor, but the erosion of the posterior clinoid processes and the floor of the sella

is more consistent with a suprasellar cyst. Unfortunately, the original films have been destroyed, so that we have to depend on the original interpretations without visualizing the films ourselves. No mention is made of calcification in the tumor area; this occurs in about three fourths of the cases of suprasellar cysts. We have to assume that it was not present. Since it is stated that the pineal body was not definitely calcified, it is likely that calcification was looked for in the region of the tumor.

The visual-field defects are stated to be more regular with a chromophobe adenoma than they are with a suprasellar cyst. In this patient, the lesions were quite consistently the same—bitemporal hemianopsia—and, hence, are in favor of adenoma.

The pathological findings at the first operation contribute some data to the differential diagnosis. The presence of a cyst favors a craniopharyngioma but does not exclude a chromophobe adenoma. Although the former is usually cystic, it may be solid; on the other hand, degeneration of an adenoma or hemorrhage into it is not uncommon. The brown fluid obtained by aspiration of the cyst might have occurred with either lesion. It would be interesting to know if crystals of cholesterol were found in this fluid, as might be expected in either lesion since they are both of epithelial origin. The presence of dense connective tissue and of large thin-walled vascular channels without epithelium suggests the stroma of a chromophobe adenoma; however, no strands of cells are described. We can more easily interpret these findings as the tough capsule of a suprasellar cyst; however, the epithelial lining of the cyst was not found.

In summing up the evidence, I believe that the most likely guess regarding the nature of the lesion is craniopharyngioma. The sequence of events was presumably as follows: an episode of acute lead poisoning; one year later, a craniopharyngioma became active and expanded to exert pressure on the optic chiasm, anterior pituitary function being adequate; first operation, a large part but not all the craniopharyngioma being removed; an interval of four years without symptoms; the craniopharyngioma again increased in size sufficiently to cause pressure on the optic chiasm and also destruction of most of the pituitary gland; an interval of two years before the second operation, with repeated evidence of underfunction of the anterior pituitary gland (panhypopituitarism) accompanied by attacks of hypoglycemia; and second operation, a large craniopharyngioma tumor mass being found that pressed on the optic chiasm and had destroyed most, *but not all*, of the pituitary gland. Some

normal anterior pituitary tissue was still present in all probability to account for the normal insulin-tolerance test.

CLINICAL DIAGNOSES

Pituitary cyst.
Panhypopituitarism, with marked adrenal insufficiency.
Circulatory failure (terminal).

DR. REIFENSTEIN'S DIAGNOSES

Craniopharyngioma, pressing on optic chiasm and having destroyed most of pituitary gland.
Panhypopituitarism.

ANATOMICAL DIAGNOSES

Pituitary adenoma, chromophobic type.
Atrophy of thyroid gland, parathyroid glands and testes.
Thrombosis of central adrenal vein, bilateral.
Infarction of adrenal medulla, bilateral.
Partial infarction of adrenal cortex, bilateral.
Pulmonary congestion and edema.
Pulmonary tuberculosis, healed, apical, bilateral.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was operated on most reluctantly in a final desperate effort to save his vision, after it was evident that radiation therapy was accomplishing nothing. A cystic tumor was once again visualized in the region of the pituitary gland, and the contents of the cyst were aspirated. It was not possible to remove the tumor itself. Following operation the patient, as had been feared, did not do well. He developed an extensive facial erysipelas. This was gradually brought under control with sulfonamide therapy, and he seemed to have rounded the corner. Then, suddenly, he collapsed, developed acute pulmonary edema and died within a few hours.

The autopsy proved that Dr. Reifenstein was correct in his analysis of the endocrine abnormality. The hypophysis had been extensively destroyed by tumor, but a small remnant of the anterior lobe could be recognized. There was atrophy of the thyroid gland, which weighed only 9 gm. and showed, on microscopic examination, extensive fibrosis and lymphocytic infiltration. The parathyroid glands showed marked fatty replacement of the parenchyma, and the testes were moderately atrophic. The adrenal glands provided a surprise. Both showed fresh thrombosis of the central vein, with extensive venous infarction involving the entire medulla and inner third to half of the cortex. It seems very probable in retrospect that this bilateral adrenal infarction correlates with the sudden terminal change in the patient's condition.

The tumor of the hypophysis turns out to be a chromophobe adenoma, with extensive central degeneration and secondary cyst formation, rather than a true primary cystic tumor, such as a cranial myringioma. In checking back over the clinical record, I find that two determinations of the 17-ketosteroids were done but for some reason were not reported until after the patient's death. The figures of 2.0 and 2.8 mg. per twenty-four hours were obtained, which are exactly in the range that Dr. Reifenstein predicted.

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NAVAL MEDICAL OFFICER PROCUREMENT

Perhaps, as intimated in a letter appearing elsewhere in this issue of the *Journal*, undue emphasis has been placed on the need for medical officers in the United States Army. The fact remains that the proportional need for physicians in the Navy is just as great.

The Office of Naval Officer Procurement is located at 150 Causeway Street, Boston, and those to whom this particular branch of the service appeals can be assured that commissions will be promptly granted to properly qualified physicians and that, ordinarily, calls to active duty will soon follow.

WILLIAM HENRY WELCH AND THE HEROIC AGE OF AMERICAN MEDICINE

Dr. William H. Welch led a life of so much activity that it would at first seem impossible to give even a running account of his many interests within the covers of a single volume. The skill of the Flexners,* however, has enabled them to present an excellent picture of one of the great figures in American medicine, a man who lived at a time when rapid evolution was taking place in medical thought. The authors have seen fit to describe this as "the heroic age of American medicine." One doubts if the term "heroic" is entirely satisfactory to describe a period such as that which Welch influenced.

That Welch should have been such a great figure in medicine is surprising in view of the fact that his early leanings were toward a career as a teacher of the classics. To be sure, his father, uncles, grandfather and great grandfather had all been country doctors in Connecticut. Medicine was indeed a tradition in the family, and the father naturally expected his gifted son to follow in his footsteps. Moreover, there was much in common between them, as one can judge by the delightful account of the country doctor given in this volume. Few pictures have been more exquisitely drawn than the description of the daily life of Welch's father, who was close to the people not only as their medical adviser but also as their true friend and counselor. The characteristic of doing so much work at night, moreover, was inherited by his more talented son.

Welch went to Yale, where he had a brilliant career both as a student and as a popular man. He was taken into Skull and Bones, the highest honor his fellow students could give him. Always interested in the classics, young Welch was tempted for years to teach school, but his father kept urging him to take a medical course and envisaged his son as his successor in country practice at Norfolk. Bending to his father's desire, Welch entered the College of Physicians and Surgeons in New

*Flexner, S., and Flexner, J. T. *William Henry Welch and the Heroic Age of American Medicine*. 539 pp. New York: The Viking Press, 1941.

York City in 1872. There, during his second year, he earned his first microscope for the best report on Seguin's lectures on nervous diseases. Because the lectures were held in the middle of Saturday afternoons, they were not well attended, but Welch considered them the best lectures in the curriculum and got his microscope, at that time something of a novelty. There were no laboratories for students in the medical school, and although a few professors used microscopes, it never occurred to them to pass their knowledge on to the undergraduates. Welch learned his first pathology from Delafield, but he soon found that if he wished to go beyond the simplest rudiments of histology, he must study abroad. After his graduation, in 1876, therefore, he took his first trip to Europe. He worked in the laboratories of Germany and France, being particularly impressed by the work of Cohnheim, who gave Welch his first chance to do experimental work. It was this work on edema that led to Welch's original paper on the subject, published in March, 1878, just after he returned to America.

Fired by an enthusiasm for laboratory investigation, he sought a post with Delafield in the College of Physicians and Surgeons. There was no space available, however, for Welch to set up a laboratory, and after a long series of negotiations, he finally obtained his desired room in Bellevue Hospital Medical College. He somehow acquired six antique microscopes and, by May, 1878, had six students working on pathologic specimens. Thus began scientific laboratory instruction for medical students in America, an accomplishment that will be regarded in the future as Welch's greatest contribution to medical advance in this country. Slowly, he increased his laboratory, and his fame extended beyond the borders of New York. Finally, the offer came to go to Baltimore, in connection with the founding of the Johns Hopkins Hospital and, subsequently, of the medical school. It was difficult for young Welch to leave New York, and his decision was certainly not made easier by the fact that his oldest and closest friend, Frederic S. Dennis, used every inducement to keep him there.

At last, the rift came, and the friendship was broken off by Dennis, much to Welch's grief. He was deeply disillusioned by the break and never again in his fifty years of association with great men did he allow anyone, either man or woman, to get close enough to him to hurt him as Dennis had done.

After another brief visit to Europe, Welch went to Baltimore, where he began his work in the fall of 1885. He was installed in a commodious two-story building quite in contrast to the so-called "laboratory" that he had occupied in New York. There, in October, 1891, Welch did an autopsy in which he showed that the tissues were filled with bubbles of gas. His bacteriologic examination led to the discovery of a new micro-organism, now known as *Clostridium welchii*. In addition to his own research, he stimulated investigation in others, and his laboratory became the center of activities in both pathology and bacteriology. The Johns Hopkins Hospital was opened in 1889, and Welch soon began to report on various diseases as they appeared in the hospital population. There was still no medical school, and to Welch fell the long and difficult task of leading the campaign for funds to establish one.

Whatever he said carried great weight, and so important had his decisions become, not only at Johns Hopkins but indeed in all medical schools in this country, that it was not strange that Mr. John D. Rockefeller and those nearest to him turned to Welch for advice in the spending of a part of the great Rockefeller fortune. Welch's name was known to Rockefeller not only for his work at Johns Hopkins but also as the founder and editor of the *Journal of Experimental Medicine*, the first scientific publication of its kind in this country. It was Welch, therefore, who laid the plans for the Rockefeller Institute for Medical Research, and his advice was widely accepted in many other fields. So great had his influence become that when two men were discussing what they would do if they had a million dollars for medical education, one instantly replied, "I should

give it to Dr. Welch." No one else in medicine in this country has ever established such a wide reputation for sound advice regarding matters of the teaching of medicine.

From his work in New York for the Rockefeller interests, he naturally spread into even wider fields and became a medical adviser to the whole nation. Few new projects were developed during the period of Welch's greatness that did not reflect, often directly, his influence. Later, he took his part in World War I, made an expedition to Japan and China and, at the age of seventy-five, established the Institute for the History of Medicine at Johns Hopkins as the culminating event in his long life.

Except for his early and close association with Dennis, Welch never had an intimate friend, and there was always about him an air of greatness, with a line of demarcation over which no one dared step. He was tolerant, pleasant and thoughtful, but always in a somewhat detached manner. Many people wished to read beneath the surface of his mind, but that was never possible. He was, however, sensitive in that he quickly reflected his environment. One notes his change of attitude toward his German teachers and friends after he had come to know American and English medicine better. He was not usually shaken, and it is said that on only one occasion, when he stepped into the post-mortem room of a soldiers' camp during the height of the influenza epidemic, did he ever appear startled and at a loss for a word. In spite of all the honors that were showered on him, he maintained his extreme modesty to the end, always going out of the way to be kind toward a junior colleague or even to a beginning student of medicine. His erudition was profound, for he could discourse on hundreds of topics in a fluent manner. He loved, nevertheless, the simple things of life, and nothing pleased him more than to join the motley crowd on a hot Sunday afternoon at the beach on Coney Island or to ride on the roller coasters with young people, with whom he immediately became friendly. He could, indeed, talk with the great without losing his

stature and converse with the lowly without embarrassment to them.

This story has been delightfully told by the Flexners. From the biography, a true picture of Welch emerges, skillfully depicted by expert hands. This is an outstanding biography of a great physician—a man not always easy to evaluate, but one whose influence in medicine will long be felt, since he was one of the greatest of four or five men who have served to make medicine in America what it is today.

MEDICAL EPONYM

POTT'S FRACTURE

This type of fracture was described by Percivall Pott (1713-1788), F.R.S., in *Some Few General Remarks on Fractures and Dislocations* (London: 1768). A portion of the text follows:

... when by leaping or jumping the fibula breaks in the weak part already mentioned, that is within two or three inches of its lower extremity . . . the inferior fractured end of the fibula falls inward toward the tibia, that extremity of the bone which forms the outer angle, is turned somewhat outward and upward, and the tibia having lost its proper support, and not being of itself capable of steadily preserving its true perpendicular bearing, is forced off from the astragalus [*sic*] inwards, by which means the weak bursal, or common ligament of the joint is violently stretched, if not torn, and the strong ones, which fasten the tibia to the astragalus and os calcis, are always lacerated, thus producing at the same time a perfect fracture and a partial dislocation, to which is sometimes added a wound in the integuments, made by the bone at the inner angle. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY: FATAL ANAPHYLACTIC SHOCK RESULTING FROM PITUITARY EXTRACT

A forty-two-year-old primipara, whose past history was irrelevant, entered the hospital with pneumonia when about three months pregnant. The medical history states that she had had rheumatic fever and mitral stenosis, although the autopsy did not confirm the diagnosis. Eleven days after hospital entry, during her convalescence from pneumonia, the patient spontaneously miscarried; the placenta, however, did not come away. One ampule of pituitary extract was given for the purpose

of stimulating uterine contractions to aid in expulsion of the placenta; this was followed immediately by severe shock. There was no hemorrhage. At first, the patient appeared intensely red and felt weak and dizzy, and thirty minutes later, vomiting and sweating occurred, the lips became cyanotic, and she was pulseless. She remained in a state of collapse. A transfusion of 600 cc. of blood resulted in improvement for the next seventy-two hours, but death occurred at the end of this time, following delirium and a rapid rise in the pulse, respirations and temperature.

According to the death certificate, the cause of this fatality was "pulmonary embolism." Autopsy, however, revealed pulmonary congestion, retained placenta and recent thrombophlebitis of the right femoral vein but no evidence of a pulmonary embolus.

Comment. This is a very interesting case. Fortunately, an autopsy was performed. This death must have been due to circulatory shock following the administration of pituitary extract; no other conclusion can be drawn. As stated above, the placenta was still in the uterus at the time of death.

These are not the times in which to try to revolutionize medicine, but it does seem as if there should be some means whereby cases that are autopsied may have the true anatomic diagnosis recorded on the death certificate. Too often, the pathologist's diagnosis does not coincide with that of the physician, and so long as this obtains, our vital statistics will be inaccurate.

DEATH

HARRIS—A. E. HARRIS, M.D., of Lynn, died July 11. He was in his seventy-third year.

Born in Montville, Maine, Dr. Harris received his degree from Bowdoin Medical School in 1895. He was a former member of the staff of the Lynn Hospital and a member of the Massachusetts Medical Society and the American Medical Association.

His widow and a brother survive him.

MASSACHUSETTS MEDICAL SERVICE

FIRST CONTRACT INITIAL STEP IN COMPLETE SERVICE

The public is not yet willing to buy complete medical-service contracts, according to the studies made by the Massachusetts Medical Society of the medical plans in operation in other states. Therefore, the Massachusetts Medical Service is initiating its program with a partial-coverage contract, which includes hospital surgery, obstetrics and diagnostic x-ray service.

This first contract is the initial step in evolving a complete medical-care service. Present plans indicate that the second contract will cover all

hospitalized illnesses and that the third contract will cover hospital, office and home care so far as experience proves it advisable.

This gradual approach parallels the method used in developing the Blue Cross nonprofit plan for hospital care and is based on the necessity for educating the public gradually to the need for increasing expenditure to obtain more complete services. The Blue Cross contract was sold first to the individual subscriber on the basis of three cents per day; next, the subscriber was willing to spend more to protect both himself and his wife; and finally, the subscriber learned the value of buying a more expensive contract that would protect all members of his family under eighteen years of age.

OTHER STATES POINT THE WAY

The wisdom of a gradual development of the Massachusetts plan is borne out by the experience of medical-service plans in other states, where complete coverage has met with poor public response.

In Michigan, 187,000 surgical-obstetric contracts were sold as against only 5816 contracts providing complete medical coverage. In one year alone, Michigan lost \$75,000 on complete-coverage contracts, of which \$10,000 was lost on a single employee group. California has sold only 30,000 complete-coverage contracts in six years, and only 10,000 have been sold in New York.

PREMATURE CONTRACTS UNSATISFACTORY

The premature sale of complete-coverage contracts to a public uneducated to them brings disastrous results in many instances. In some states, compensation to family physicians dropped to from twenty to sixty cents on the dollar. In other states, the medical-service corporation went into debt to maintain payments to physicians.

Buffalo, California and Michigan are selling no more complete-coverage contracts, and all the states that began with complete-coverage contracts have been forced to revert to the issuance of the surgical-obstetric contract. "The surgical-benefit contract is more or less predictable from an actuarial basis," writes Philo Nelson, general manager of the California plan, "and is the soundest to begin with." John Mannix, executive director of the Michigan Hospital Service, who is closely affiliated with the Michigan Medical Service, states, "From the experience of Michigan, partial coverage is the only approach that is reasonable." The wisdom of the partial-coverage contract is further confirmed in a preliminary report made by the Superintendent of Insurance of the State of New York, who says: "A greater appeal seems to exist for surgical benefits only than for general medical coverage. This is due, perhaps, to the possibility of being con-

fronted with much more substantial bills for surgical services than for general medical expense. It is understood that the plans contemplate experimenting to a greater extent in this field."

By enthusiastically and actively supporting the program of the Massachusetts Medical Service, physicians of the State may help to avert the appearance, in Massachusetts, of a bill similar to the following, which will be supported next year by the New York Insurance Commission unless the medical profession of that state takes active steps:

"A hospital corporation may, by amendment of its charter, acquire the power to supplement its contracts for hospital service by provision for the furnishing of indemnity against physicians' fees for surgical and obstetrical care rendered" (Hampton Bill, New York Senate No. 1273 In. 1054).

WAR ACTIVITIES

OFFICE OF CIVILIAN DEFENSE

HOW TO PROTECT YOURSELF AGAINST GAS

Two recent operations letters dealt with the establishment of improvised decontamination stations and with the organization of decontamination services, respectively. This letter deals with personal protection against gas.

The following information on war gases is supplied by the United States Office of Civilian Defense for general publication because of the possibility that such gases may, at some time, be used by the enemy. If people will remember a few simple facts, they will have no unreasonable fear of this agent.

* * *

War gases stay close to the ground, for they are heavier than air. To get out of a gassed area, simply walk against the wind or go upstairs.

Gas is irritating and annoying to the eyes, nose, lungs and skin, but it is usually harmless if you do not become panicky but promptly leave the gas area and cleanse yourself. A soldier must put on a mask where it is necessary to remain in the contaminated area, but a civilian can go up on the second or third floor and literally ignore it, if the windows are kept closed.

If the gas should get on your skin, you can prevent it from doing much harm by sponging it off as quickly as possible with a piece of cloth, such as a handkerchief, and applying some neutralizing substance, followed by a thorough bath, preferably a shower, with common laundry soap and water.

If you are indoors, stay there with doors and windows closed, and go up to the second or third story. Stay out of basements. Turn off air-conditioning equipment, and stop up fireplaces and any other large openings.

Some gases are spread as oily droplets, which blister and burn the skin and eyes. If you are outside when gas is used do not look up. Tear off a piece of clothing or use a handkerchief to blot any drops of liquid from your skin and throw the contaminated cloth away. Blot; do not rub, as rubbing will spread the liquid. Then go home, if it is nearby, or to the nearest place where you can wash immediately with soap and water and cleanse yourself in the following manner:

(1) Remove all outer clothing outside the house, since

gas can be transmitted to others from contaminated clothing. Put it preferably in a covered garbage pail.

(2) Apply one of the following effective household remedies to the part of your skin that has been contaminated: Chlorox or a similar household bleach (for mustard gas); peroxide of hydrogen (for Lewisite); a paste or a 2 per cent solution of baking soda (one tablespoonful to a quart of water), if you have no bleach or peroxide. If you do not know the gas, use both bleach and peroxide. Keep the bleach and the peroxide out of the eyes. *Do not waste time looking for these remedies: bathe immediately if they are not at hand.*

(3) After entering the house, wash the bleach or peroxide from the hands with laundry soap and water and then wash the face. Remove the underclothing, place it in a covered garbage pail and enter the bathroom.

(4) Irrigate the eyes with large amounts of a lukewarm 2 per cent solution of baking soda (one tablespoonful to a quart of water), or else with plain water. Use an ordinary douche bag or an eye irrigator. If you do not have these, let plain warm water pour into the eyes from the shower, washing them thoroughly. Do not press or rub the eyes.

(5) Lastly, take a shower, using laundry soap and hot water.

(6) If the nose and throat feel irritated, wash them out with the baking soda solution.

(7) If the chest feels heavy and oppressed, if you have any trouble breathing or if cigarette smoke becomes distasteful, lie down and stay perfectly still until a physician sees you.

(8) If blisters develop, be careful not to break them and call a physician.

Remember:

Soldiers require gas masks because they must remain in the contaminated area. Civilians can get out of the gassed area or get above the level of the gas, where they do not need gas masks or protective clothing.

Injured persons who are gassed require decontamination before they can be admitted to hospitals. All other civilians can best prevent any serious injury by promptly helping themselves in the manner outlined, using a kitchen or bathroom, laundry soap and water, and a few materials found in every household.

CORRESPONDENCE

NAVAL MEDICAL OFFICER PROCUREMENT

To the Editor: The imminent conscription of all medical skills for the war effort has been amply outlined and urgently stressed in your columns, especially in the issue of July 2. There has been a tendency among physicians to interpret this need and opportunity as one of service in the Army. Indeed, rumors have come to my attention that doctors were no longer needed in the Navy and that commissions in the Naval Reserve were not being granted or, if granted, the call to active duty was likely to be deferred.

All of us recognize the larger numerical need of the Army, but the proportional need of the Navy remains just as great. Current directives inform us that quotas of medical officers of the Naval Reserve have been greatly extended and that many more applications for commis-

sions should be obtained as promptly as possible. Furthermore, physicians commissioned in the Naval Reserve may ordinarily anticipate prompt call to active duty.

The Office of Naval Officer Procurement is located on the sixth floor of the North Station Office Building, 150 Causeway Street, Boston. Captain C H J Keppler is in charge, and the office is open daily from 8 00 a m to 4 30 p m to receive applications or to supply information. If seriously interested local medical societies, hospital staffs or other medical groups at a distance from Boston desire a representative of the Naval Reserve Medical Corps as a speaker, every effort will be made to accommodate them.

LIEUT COMOR ROBERT S PALMER, MC V(S), USNR
Office of Naval Officer Procurement
150 Causeway Street
Boston

REFUGEE PHYSICIANS'

To the Editor We, the undersigned as physicians who have come here from foreign countries in recent years take note of the letter from Dr P C Zanfagna, president of the Greater Lawrence Medical Association, published in the June 18 issue of the *Journal*.

The whole tenor of this letter is reminiscent of familiar propaganda attacking groups that are weakest from an economic and legal point of view, groups to which we as immigrant physicians, belong.

Dr Zanfagna refers to Massachusetts as a 'dumping ground for physicians not wanted elsewhere'. In the course of recent immigration, approximately 200 immigrant physicians obtained licenses in Massachusetts. Not more however, than 100 are in general practice, and they represent 126 per cent out of the total number (7889) of registered physicians. In 1942, immigration stopped.

The Board of Registration in Massachusetts is accused in this letter of licensing aliens whose class of school and educational background cannot be verified. This is not true, since practically all these immigrant physicians graduated before 1933, when the status of their schools was known and had been verified by the American Medical Association and National Board of Medical Examiners. The same scientific and ethical qualifications were demanded of them when they took their state board examinations in Massachusetts as are required of native physicians. When it is realized that the great majority of these physicians, who are between forty and sixty years of age, successfully passed the examinations despite the mental disaster they had experienced and the language hurdle they had to overcome, the allegation that they are ignorant and incompetent is nothing less than absurd. Most of these men had been in practice for fifteen to twenty years before they came to this country. The implication that spies or saboteurs can be guarded against by requiring citizenship is a condition of licensure strikes us as bordering on the preposterous.

The immigrant physician is not a little confused by the fact that while the shortage of physicians mounts steadily, he willing to serve in any capacity and not wanting to impose on native physicians or compete with them, stands waiting. Let him be taken into the Indian Service or into a medically unmanned area in any state. He will go gladly if given the opportunity.

We agree that immigrant physicians should do military service along with native physicians, to state, however, that Major Seeley does not want these men to treat our boys is untrue. A number of the undersigned and others went to the Army Base on the very first day of

the war to offer their services in any capacity, they were informed that the law prohibits the commissioning of non citizen physicians. Practically all immigrant physicians responded to the request of the Procurement and Assignment Service and offered their services. The undersigned physicians, speaking on behalf of the majority of immigrant physicians in Massachusetts, take this opportunity to appeal to the Massachusetts Medical Society and the American Medical Association for help in becoming acceptable for military service, and whenever and wherever they may be needed. This is the least they can do to show their gratitude to this country, which gave them a haven of refuge and a new home.

Perhaps, those whose ancestors came to these shores as aliens should look back to those times and compare for themselves the former hospitality with what is extended to us by some of them today.

J FISCHER MD
J FISCHMANN, MD
K GOLDSTEIN, MD
L HESS MD
J IERSHEIMER, MD
G LEPEHNE, MD
M M NOTHMANN MD
S J THANNHAUSER, MD

Boston

REPORTS OF MEETINGS

MASSACHUSETTS TUBERCULOSIS LEAGUE

On April 9, the Diabetes Committee of the Massachusetts Tuberculosis League met at the Myles Standish Hotel Boston. Under the leadership of Dr Elliott P Joslin, this committee has worked steadily against diabetes since its founding in March 1935. The committee is very small, and its annually invited representatives are among those persons most interested in diabetes in the eleven largest hospitals of Boston.

Since the majority of deaths from diabetes occur in these hospitals, it was believed that the physicians concerned should be the ones to study most intensively prevention and treatment seeking to correct their own mistakes than to initiate, as was done in some other cities, a popular organization to combat diabetes. Various procedures have developed in combating diabetes as a result of repeated interchange of experiences on every phase of the treatment in the hospitals of Boston. Successive yearly meetings have recorded improved results.

Through the years, the physicians representing the hospitals have attempted to meet and discuss diabetes with physicians whose cases sent to the hospital have proved serious or obscure.

To the members of this committee come interesting bits of literature on diabetes. At the meeting was presented Volume I of the *Proceedings of the American Diabetes Association*, the first annual meeting having been held at Cleveland on June 1, 1941. Also presented was the first copy of *Diabetes Abstracts* issued in January, 1942 a quarterly of the new American Diabetes Association. These abstracts, said by the physicians to cover the field splendidly, are produced at the expense of the Eli Lilly Research Laboratories, which were already equipped to gather this material.

The Diabetes Committee consists of Dr Elliott P Joslin chairman, Dr Herbert Lombard, Dr Alton S Pope, Dr Francis P Denny, Dr Charles F Wilinsky, Arthur J Strawson, secretary, and Dr Henry D Chadwick, ex officio.

PLYMOUTH DISTRICT MEDICAL SOCIETY

The annual meeting of the Plymouth District Medical Society was held at the Bridgewater State Farm on April 16, 1942. The minutes of the previous meeting were read by Dr. R. C. McLeod.

Dr. R. A. Kruger reported small progress in the investigation of the group health insurance for the members of the society. At least one company would require 50 per cent of the membership to join. All policies would be on an annual basis and cancellable at the discretion of the company at the end of one year. It was Dr. Kruger's opinion that none of the companies were really anxious for this type of business. It was voted to poll the entire membership as to its wish to investigate the matter further. Dr. J. J. McNamara offered to present an insurance man at a later meeting to explain further.

The officers for the ensuing year were elected as follows: president—C. D. McCann; vice-president—E. L. Perry; secretary—R. C. McLeod; treasurer—A. L. Hurlburt; councilors—W. H. Pulsifer (nominating), P. H. Leavitt (alternate, nominating), J. E. Brady, W. T. Hanson, Charles Hammond, P. B. Kelly, G. A. Moore and D. W. Pope; censors—W. T. Hanson (supervising), J. H. Dunn, G. A. Buckley, H. F. Pierce and A. W. Carr; orator—W. C. Gould; librarian—J. H. Weller; and commissioner of trials—J. A. Carriuolo.

Dr. G. A. Moore, the retiring president, thanked the faithful members for their attendance and help throughout the year, and presented small tokens to the members present. Dr. P. H. Leavitt gave a report on progress in the Society's medical-insurance program. Dr. Moore presented Dr. F. E. Wheatley as orator. Dr. Wheatley also was orator twenty-five years ago and remarked that following both appointments a world war had occurred.

Dr. Wheatley's paper concerned roentgen-ray therapy. As early as 1904 in Boston, Dr. Francis Williams wrote a book on x-ray treatment, but early doses were uncontrollable. In 1914, the Coolidge tube, which allowed dosage regulation, was introduced. It was found that high-voltage machines give off as many nonpenetrating rays as low-voltage ones, and require screening with aluminum or other metals. In the early 1920's, potentials as high as 200 kilovolts were available. Huge doses under high voltage were thought lethal to new growths, but soon proved lethal to healthy tissues also. Repeated divided doses afford a better chance for the normal tissues to recover. Radiation for deep therapy is still in a chaotic state, since high-voltage treatment has been a disappointment. In inflammatory processes of acute nature, many small x-ray doses do very well. Precancerous lesions are best treated by small doses. A slowly growing lesion often requires heavier total dosage than the rapidly growing type. Advanced and hopeless cases of deep cancer can only be damaged, and such sequelae as burns and x-ray sickness may be worse than the disease itself, and may help to kill the patient sooner. The pros and cons of x-ray exposure before or after breast amputation are still under discussion. Some believe that perhaps 10 per cent more patients live five years after having x-ray treatment. In other constitutional conditions, such as leukemia, Hodgkin's disease and splenomegaly, rapid and massive dosage is a poor choice. Weaker doses have accomplished much more, and no fatalities have resulted for two or three years after treatment. The previous conception of x-ray therapy has been correlative to the idea of a cure of malignant tumors. In the speaker's opinion, more attention should be given to the palliative effects.

EDWARD L. PERRY, M.D., *Reporter*

BOOK REVIEWS

Shock Treatment in Psychiatry: A manual. By Lucie Jessner, M.D., Ph.D., and V. Gerard Ryan, M.D. With an introduction by Harry C. Solomon, M.D. 8°, cloth, 149 pp. New York: Grune and Stratton, Incorporated, 1941. \$3.50.

A new kind of treatment for psychiatric disorders has been developed since 1928, when Sakel first began giving insulin in doses sufficient to produce hypoglycemic states. Insulin therapy was subsequently augmented, although not entirely replaced, by the Metrazol convulsive treatment of von Meduna, in 1933. The third method,—electric convulsive therapy,—introduced by Cerletti and Bini in 1937, is now extensively used, and in many clinics has displaced the more dangerous, less well-controlled shock treatment by insulin or Metrazol.

This small but excellent book covers the historical data, the details of the use of the three methods and their dangers, the selection of patients, the theoretical considerations and the effect of shock treatment on the course of various mental diseases. The manual is timely, accurate, sufficiently detailed and soundly written. There is a voluminous but selected bibliography. The price charged for a book of less than one hundred and fifty pages is quite high.

Body Mechanics in Health and Disease. By Joel E. Goldthwait, M.D., LL.D., Lloyd T. Brown, M.D., Loring T. Swaim, M.D., and John G. Kuhns, M.D. With a chapter, "The Heart and Circulation as Related to Body Mechanics," by William J. Kerr, M.D. Third edition, completely revised and reset. 8°, cloth, 316 pp., with 121 illustrations. Philadelphia: J. B. Lippincott Company, 1941. \$5.00.

The main theme of this work is the effect of poor body mechanics on the various systems of the body. It is easy for one to appreciate the influence of improper posture on the joints and their supporting structures. Just as important, but far less obvious, are the secondary effects on digestion, circulation and respiration. The authors discuss the diagnostic features of poor body mechanics and outline the proper treatment for the various types.

This book deals largely with end results and, by emphasizing the evils, points the way to prophylactic care in early life, when habits are formed. A good bibliography is appended for more detailed study of the particular problems.

Edith Cavell. By Helen Judson. 8°, cloth, 288 pp. New York: The Macmillan Company, 1941. \$2.50.

Edith Cavell's tragic story has often been told, but nowhere better than in this work by an author who has made a profound study of Miss Cavell's whole career. The book is well written and brings out clearly Miss Cavell's character, the type of work that she was engaged in as a nurse, the reasons for her being apprehended by the Germans and the details of her execution. Although much of this material has been known for years, Miss Judson has added new details of historical importance. The author, moreover, has been careful not to emphasize the emotional effect of Miss Cavell's death; she has written a straightforward account such as, one presumes, Miss Cavell would have approved herself. There is no hatred or bitterness in the book, and the standard followed is similar to that set by Miss Cavell in her famous remark: "I know that patriotism is not enough; I must have no hatred and no bitterness toward anyone."

(Notices on page ix)

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THE PROBLEM OF CERTAIN TROPICAL DISEASES IN THE WAR*

HENRY E. MELENEY, M.D.†

NEW YORK CITY

TROPICAL medicine has not been one of the major specialties of American medicine, although it has been a field in which some of the most notable achievements have been made by American physicians. A few universities, especially Harvard and Tulane, have had departments of tropical medicine, but the greatest activity in this field has been carried on by the United States Army, Navy and Public Health Service and the Rockefeller Foundation. The interest of most medical schools and practitioners has been absorbed by their local problems, which have been quite different from those of the tropics. Now we are faced with the necessity of sending large numbers of troops to countries where tropical diseases are the chief hazards, and medical officers, whose duty it is to keep the troops in fighting condition, are confronted with the problem of diagnosing, treating and preventing diseases that have not been a part of their training and experience. Those of us who remain in civilian practice may also be faced with similar problems when the troops return to civil life. It is therefore appropriate to call attention to some of the problems in tropical medicine that our present national effort involves.

MALARIA

The most important of these problems is malaria, which, clinically, really comprises three separate diseases—the benign tertian and quartan types, which cause great disability but few deaths, and the malignant, tropical, estivoautumnal type, which may simulate a wide variety of other diseases, is often fatal and is frequently associated with severe complications, such as blackwater fever and profound anemia. Diagnosis is sometimes difficult because of the bizarre manifestations of this dis-

ease, and also because the parasitized red blood cells stick to the walls of capillaries during the second twenty-four hours of the asexual life cycle and may not be found in the circulating blood. The important thing is for the physician to have malaria constantly in mind in every case of illness in the tropics, and to make repeated blood examinations on consecutive days until malaria is diagnosed or definitely excluded.

The treatment of malaria is not the simple procedure that it is often thought to be. Even after a supposedly complete course of treatment with quinine or Atabrine, relapses occur in about 50 per cent of cases of tertian and quartan malaria, and in about 20 per cent of cases of estivoautumnal malaria; and in estivoautumnal malaria, the early relapse may be fully as severe as the first attack. We do not yet know whether relapses are due to the continuation of the asexual cycle in tissues outside the general circulation, such as the splenic pulp, where the parasites are protected from a sufficient concentration of the drug to kill them, or whether they are due to a so-called "exocrythrocytic form" of the parasite that multiplies in the reticuloendothelial cells of the body. The tendency in the last few years is to use short, vigorous courses of treatment for the acute attack and to treat the relapses as they occur; but many authorities still believe that the treatment should be continued for eight to ten weeks, a procedure that is very difficult to carry out in troops on active service.

The prevention of malaria in troops by the prophylactic use of quinine or Atabrine is unsatisfactory for several reasons. It requires an enormous amount of these drugs, which are now difficult to obtain. It requires responsible persons to administer the drugs to troops individually, to be sure they are taken. The drugs cause aviators to perform abnormally at high altitudes. Finally, these drugs are not true prophylactics, since they have no lethal effect on the sporozoite introduced by

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†Professor of preventive medicine, College of Medicine, New York University.

the mosquito, and only postpone the clinical disease in infected persons until the drug is no longer administered.

The prevention of malaria by the control of mosquitoes in the tropics is also a tremendous problem. Even in fixed military establishments, it requires expert organization, constant vigilance and great expense. When troops are operating in the field in endemic areas, it is impossible to protect them from infection. Bed nets are poor substitutes for adequate screening, and mosquito repellents have not been developed to a point where they will protect persons from mosquito bites longer than forty-five minutes under sweating conditions.

Even in our fixed bases in the Caribbean, the control of *Anopheles* breeding may be a serious problem. In one area, for instance, an important malaria vector breeds in the leaves of a plant growing high in the trees. Another problem is the transportation of dangerous species of *Anopheles* by airplanes and fast ships across the ocean. In 1930, *Anopheles gambiae*, the chief vector of malaria in West Africa, was discovered on the north-eastern coast of Brazil and soon caused a devastating epidemic in its new habitat. By strenuous and costly efforts, the Brazilian government and the Rockefeller Foundation apparently eradicated the mosquito from the area in 1940, but the threat of its reintroduction is again indicated by the recent finding of this mosquito on three occasions in airplanes reaching Brazil from Africa.

Troops and civilians returning from the tropics to nonendemic areas of malaria in the temperate zones will undoubtedly bring with them latent and chronic malarial infections, which the medical profession must be on the alert to diagnose and treat to avoid the establishment of the disease in the civilian population. This happened in England after World War I, and may occur even in New England after the present war.

ENTERIC DISEASES

Typhoid fever was well controlled by vaccination and sanitation in American forces during World War I, but it was not entirely eliminated, especially in France, where troops operated in unprotected areas. During the present war, with troop movements much more rapid and with large numbers of them operating in the tropics, we must expect a higher incidence of typhoid fever unless emergency sanitation is more efficient than in the last war, and unless the troops are educated to protect themselves from polluted water and food under the most trying circumstances.

The dysenteries and diarrheas were formerly the most prevalent and disabling diseases among troops in camp and on the march. In World

War I, although these diseases had dropped to seventh place among the causes of illness in the American army, bacillary dysentery was an important cause of illness during the active summer campaigns in France. In the Philippines, even though there was no fighting, the diarrheal diseases caused by far the highest admission and death rates among our troops. There is at present no specific preventive against either bacillary or amebic dysentery, and although we now have effective drugs for the treatment of both conditions, some cases, especially those of amebic infection, are likely to be insufficiently treated under war conditions and may lead to chronic disability or become sources of infection among the civilian population after the war. Drug prophylaxis of both bacillary and amebic dysentery has been suggested, but the expense and labor entailed in such a procedure make it impractical except in the presence of an epidemic, and in such a situation, sufficient quantities of the drugs would probably not be available. Here again, prevention must depend solely on the most rigid sanitation and education of the troops.

The mild epidemic diarrheas must not be forgotten, since they may disable essential units during crucial periods. We now recognize *Salmonella* diarrhea, staphylococcus-toxin diarrhea and water-pollution diarrhea as frequent epidemic diseases among the civilian population. Although they may occur in any latitude or in any season, they are more frequent during warm weather. The greatest care in the handling and preparation of meats, salads, milk and pastries must be observed to prevent food-borne epidemics. One such epidemic was reported among troops who ate insufficiently cooked bread during World War I. Water-pollution diarrhea is perhaps likelier to occur as scattered cases in soldiers drinking from polluted sources than as an epidemic, but its possibility must be kept in mind wherever public water supplies are used, and the danger of a typhoid epidemic, following it after the usual incubation period, must always be remembered.

It may seem farfetched to mention cholera as a possible problem in our war effort. But it must be remembered that the disease is endemic in India and Central China, that there was an epidemic of it in the Philippines as late as 1934, and in the coastal regions of China in 1938, and that it is a constant threat in the Malay Peninsula and Burma. It is reported to be prevalent at the present time in Greece, and might spread easily to the Balkans, Russia and other near-by countries. Although a vaccine against it is available for the use of our military forces, protection is only partial and of short duration, and requires repetition in the endemic areas every six months.

With the destruction of cities and the migration of refugees, it will be surprising if severe epidemics do not occur, and the possible operation of our troops in devastated areas may expose them to the disease.

MISCELLANEOUS DISEASES

Epidemic louse-borne typhus fever is, of course, one of the greatest threats to armies, prison camps and starving populations in the cooler climates, but it has also been epidemic in Spain during the past two years and is almost constantly present in North Africa and China. Within the last few years, murine typhus in rats has been found to be an endemic disease in most parts of the world, being transmitted to man by the rat flea. There is only a questionable difference between the murine and the epidemic louse-borne strains of the typhus rickettsia, and evidence has been brought forward, especially from China, that the murine disease in man can give rise to louse-borne epidemics. The delousing of troops was a major activity of the medical department of the American army in France during World War I, and the maintenance of a louse-free army during the present war will require constant alertness and efficient delousing facilities. Although a vaccine against typhus has been developed, its protective power is questionable, and the results of further experimentation and of trial in large groups of exposed persons must be awaited before any statement can be made concerning its value.

Relapsing fever must not be forgotten as a louse-borne disease, which either accompanies typhus fever or appears as an independent epidemic. The tick-borne variety of the disease is widely distributed in Africa and Central and South America, and even occurs in the western United States. It must be kept in mind among troops operating in these areas.

The war in the Orient has centered about areas where bubonic plague is most prevalent. Java, Malaya, India and Central and South China have found the disease a serious problem during the present century. There are indications of its increase to epidemic proportions in certain parts of China at the present time, and with the destruction of cities and consequent migration of rats, it will not be surprising if the disease gets out of control over wide areas. Wherever there are bubonic cases, a certain number of pneumonic cases occur, and under conditions of crowding, both of troops and civilian populations, the threat of pneumonic epidemics may be present. Even in our own country, the so-called "sylvatic plague" in ground squirrels and other wild rodents has advanced from the Pacific Coast across the continental divide and is now moving

slowly toward the central states. Although this will probably not be a military problem, it is a serious problem to the United States Public Health Service, whose functions are now put under stress by the war effort. Recent discovery that the sulfonamide drugs are of value in the treatment of bubonic plague is hopeful in view of the high case fatality rate of the disease. In prevention, vaccine is thus far only partly protective but is being held in readiness for troops likely to be exposed. Rat control is one of the most difficult procedures, even under the most favorable circumstances, and will hardly receive attention in any except the most seriously affected plague areas in the Orient while the present struggle lasts.

The campaign against yellow fever has fortunately eliminated epidemics of this disease in the Western Hemisphere, but the discovery of its endemic existence in the jungles of South America makes constant vigilance necessary to prevent it from extending to cities where the *Aedes aegypti* mosquito can start epidemics. In Africa, it is still epidemic as well as endemic, and its presence in the Egyptian Sudan leads to the possibility that it might be transported in infected mosquitoes to India. In the past, lack of rapid transportation from Africa has probably been the only reason why the disease has never occurred in Asia. If such a spread should now occur, the result might be one of the greatest calamities of the war. The most careful inspection and fumigation of all airplanes before leaving endemic areas and after arriving at their destinations constitute the only method by which Asia can be protected from this invasion. Vaccination against yellow fever apparently affords complete and permanent protection, and must be performed on all persons going to or through endemic areas.

Dengue fever, which may be considered a mild relative of yellow fever, is caused by a filterable virus having the same incubation and infectious periods in mosquito and man, is transmitted chiefly by *A. aegypti* and exists in nearly all parts of the tropics. It may cause disabling epidemics among troops at crucial periods. Unfortunately, one attack produces only temporary immunity so that subsequent exposure may again lead to further epidemics in the same group.

A number of other diseases should be mentioned to complete the picture of the hazards to which our troops may be exposed in the tropics. Although none of these will occur in epidemic proportions or even in high incidence, they may present diagnostic problems to medical officers or, after the war, to civilian practitioners.

Leprosy, yaws, leishmaniasis in its visceral form, kala-azar, or in its Oriental or American cutaneous

form, African trypanosomiasis, schistosomiasis, the blood-fluke disease, filariasis and hookworm are major diseases in some parts of the tropics and must be constantly kept in mind.

Mention should also be made of the effects of tropical heat on the white man. In addition to the acute conditions of sunstroke and heat stroke, and the salt loss from excessive perspiration, there are more insidious conditions that often produce disability and are not well understood. Dietary demands are different from those in the temperate zones, with a tendency to a higher relative intake of carbohydrates, which may predispose to intestinal infections. This may also be related to a greater demand on the part of the body for certain vitamins, particularly those of the vitamin B complex. In this connection, there is some evidence that thiamine requirements are higher in the tropics. Sprue is undoubtedly a deficiency disease in some way related to this field.

There is also evidence that the endocrine glands, particularly the adrenal glands, may not function normally in the tropics, as manifested by asthenia and low blood pressure. All these disturbances may contribute to the exhaustion that so often drives the white man home from the tropics, or makes him lose the energy necessary to fight a vigorous campaign there.

This brief summary of some of the medical hazards of the tropics indicates clearly that the medical officers of our armed forces should be much better prepared for service in these areas than most of them are. The Army and Navy are giving short courses in tropical and parasitic diseases to a limited number of the medical officers going to the tropics, and two medical schools have given voluntary courses to officers awaiting orders. This, however, is an emergency procedure and cannot possibly provide such knowledge to all the medical officers who should have it. Our lack of interest in the tropics and the scarcity of tropical diseases in this country have led to the almost total neglect of instruction in tropical medicine and parasitology in most of the medical schools of the country. It is not too late, however, to remedy this situation for the benefit of our present medical students, who may see service in the tropics before the war is over. Already such instruction is being organized in certain medical schools, and it should be in all of them. After the war, our interest in the tropics and the possibility of the occurrence of more tropical diseases in this country, because of returned troops and greater travel, should lead to permanent provision for adequate undergraduate and postgraduate instruction in this vital field of medicine.

THE PRESENT PROGRAM FOR THE IMMUNIZATION OF MILITARY PERSONNEL*

JOHN F. ENDERS, PH.D.†

BOSTON

RECENT advances in our knowledge of pathogenic bacteria as antigens and in the nature and immunologic properties of viruses have led to the development of a number of new procedures for the production of active immunity.

The adoption of these and the retention of the tried and true vaccinations against smallpox and typhoid fever by the United States Army and Navy, although usually making the first week or so of the recruit's service a far less agreeable period than it was heretofore, will undoubtedly help to preserve his life and maintain him in fighting trim on those fronts, ranging from the Arctic to the tropics, where he seems destined to fight.

My purpose is to review briefly such procedures as are now in routine use in both major arms of

our forces and to comment on certain improvements that might be made in some of them according to investigations now in progress.

* * *

Smallpox

There is little to be said concerning vaccination against smallpox that is not familiar to everyone. In both services, it is required for all personnel and is effected immediately on induction and every three years thereafter in the Army and every four years in the Navy. Under special circumstances, such as departure for an active theater of operation, vaccination must be carried out unless it has been done within the preceding twelve-month period. During the last few years, vaccine virus propagated in tissue cultures or in the developing hen's egg has been suggested as a substitute for calf lymph. Such preparations, however, have not proved satisfactory, and the traditional material is employed

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From the Department of Bacteriology and Immunology, Harvard Medical School and School of Public Health.

†Assistant professor of bacteriology and immunology, Harvard Medical School.

exclusively among the armed forces as in civilian life.

Stress is laid on the use of the proper technic for introducing the virus into the uppermost layer of cells in the dermis. The medical officer also must be thoroughly familiar with the three types of reaction that may occur—immune, accelerated and primary. If no reaction or a doubtful reaction is obtained, vaccination must be repeated several times with virus of high potency to ensure that a genuine immunity exists.

Typhoid and Paratyphoid Fevers

Antityphoid vaccination is, of course, also mandatory in both services. The important observations of Grinnell,¹ published in 1932, on dissociative changes in the direction of loss of virulence and altered antigenicity that had taken place in the Rawlings strain of *Eberthella typhosa*, then almost universally employed as the source of typhoid vaccine, have led to the substitution of the highly virulent and potent antigenic P-48 strain by the Army officials. This change should definitely improve the efficacy of the vaccine.

For a time *Salmonella paratyphi* and *S. schottmülleri* (paratyphoid A and B bacilli) were omitted, but at present they are again represented in the vaccine, which contains 1,000,000,000 typhoid organisms and 250,000,000 each of the paratyphoid bacilli per cubic centimeter.

The vaccine is given in the usual three doses of 0.5, 1.0 and 1.0 cc. at weekly intervals, and the injections are attended by the local and generalized reactions of varying severity unpleasantly well known to most of us. It is possible that such variation in reaction may, in part, be attributed to the mode of administration, and it has been suggested that care should be taken to introduce the material quite superficially under the skin, first making certain that the needle has not entered a small blood vessel.

It has been found by Siler and his colleagues² at the Army Medical School that a recall, stimulating or so-called "booster" dose of the vaccine given in the amount of 0.1 cc. intradermally one year after the initial series of injections effectively restores the antibody level, and so presumably efficiently maintains resistance. On the basis of these observations, the Navy has adopted as routine the administration of an intradermal recall injection every year, although, so far as I am aware, the Army still holds to the older procedure of re-vaccinating every three years, with the exception, as in smallpox vaccination, of those persons leaving continental United States for an active theater of operations.

Since intradermal inoculation of the vaccine is usually attended by reactions of less intensity compared to subcutaneous injection, and since the antibody response is excellent, this method should come into general use in the near future.

Under present circumstances, the desirability of including the paratyphoid bacilli and possibly even other varieties in the vaccine leads to the practical certainty of severe reactions due to the presence of large quantities of unessential bacterial proteins and other constituents. The isolation of a complex carbohydrate-lipid-peptide antigen by Boivin et al.³ in France and Raistrick and Topley⁴ in England from various species of the typhoid-paratyphoid group suggested a possible method of vaccination in which the injection of a large proportion of presumably unnecessary bacterial substances might be avoided. Morgan,⁵⁻⁷ in our laboratory, has produced from the typhoid bacillus grown on a medium of known constitution an antigen similar to those described by the French and English workers. Although definitely toxic, this substance has been found to stimulate effectively the production of mouse-protective antibodies when injected in extremely small amounts into human volunteers. Thus, a comparison of the antibody levels following injection of this purified antigen with those obtained after the usual series of injections with typhoid vaccine indicates that they are about equally effective. Of particular significance is the fact that, in the quantities employed, the purified antigen gave definitely milder reactions, characterized merely by local manifestations. Obviously, much further experimentation is necessary before one should contemplate substituting chemical derivatives of this sort for the whole bacillus, but the observations I have outlined encourage such research.

Tetanus

Concerning the very important problem of the prevention of tetanus, all the evidence at hand indicates that we are in a much more satisfactory position than we were during the last war, when antitoxin was the only available prophylactic. In addition to the disadvantage of using a foreign protein,—which is so liable to induce hypersensitivity,—the brevity of the period of its effectiveness following injection represents a distinctly undesirable feature. Ramon's discovery that tetanus toxin treated with 0.3 per cent formalin and maintained at 37°C. for several weeks resulted in a product exhibiting no toxicity but strong antigenicity has given us a method of safely and conveniently inducing a basic active immunity of long duration that may be quickly enhanced, when desired, by a single stimulating dose of the toxoid.

All military personnel on induction are now immunized either, as in the Army, by three injections of the plain or liquid toxoid or, as in the Navy and Marine Corps, by two injections of alum-precipitated toxoid.

The liquid toxoid is administered subcutaneously in quantities of 1 cc. at intervals of three or four weeks, and a single stimulating dose of 1 cc. is given under normal conditions twelve months after the last of the three initial injections. In wartime, a recall dose is injected during the month prior to departure for a theater of operations, unless such departure is within a period of six months subsequent to the stimulating dose or within six months subsequent to the initial series.

An emergency dose of 1 cc. of toxoid is given to soldiers wounded or burned on the battlefield, to patients undergoing secondary operations or manipulations of old wounds, when deemed advisable, and to others incurring nonbattle wounds likely to be contaminated with *Clostridium tetani*. This emergency dose in vaccinated persons appears to replace effectively the use of antitoxin.

In the Army, a record of tetanus immunization, if properly completed, is stamped on the identification tag. To wounded men who have not received all the injections or whose vaccination record is not available, tetanus antitoxin is administered at the same time vaccination with toxoid is begun.

Although parenteral injection of toxoid is far less likely to cause anaphylactic reactions than that of antitoxin, these have occurred on the administration of toxoid to persons allergic to various materials and occasionally to those who have previously received toxoid. Accordingly, in the Army, the following precautions must be observed in carrying out the vaccination: adrenalin should always be on hand, and intradermal sensitivity tests, 0.1 cc. of a 1:100 dilution of toxoid being used, should be done on all who have a history of previous allergic manifestations, who have exhibited untoward reactions to a previous dose of toxoid and who have received toxoid in the initial immunization series after an interval longer than four weeks. When mild reactions occur in the initial series, immunization can be completed by the administration of not more than 0.1 cc. of toxoid in three or four doses at daily intervals.

To my mind, these precautions are very well worth observing, not only by the medical officer but by anyone who undertakes to administer toxoid. It should, however, be clearly understood that the percentage incidence of such reactions has in the Army been extremely low and that they have in no way interfered with the tetanus-immunization program. Most of them seem to

have been due to certain brands of peptone employed in the mediums for growing the tetanus bacillus. In the bacteriological laboratory at the Harvard Medical School, a medium has been developed by Mueller⁸ that does not include peptone and that promises to permit the production of a toxoid that should give definitely fewer reactions.

In the Navy and Marine Corps, alum-precipitated toxoid is given in two injections of 0.5 cc. each by the intramuscular route, with an interval of not less than four and not more than eight weeks. In addition, a stimulating dose of 0.5 cc. is given once a year and repeated, if possible, before the zone of combat is entered. The emergency dose of toxoid is likewise 0.5 cc. As in the Army, to persons not satisfactorily immunized with toxoid, antitoxin is given in case of necessity, at which time active immunization with the toxoid is inaugurated.

The adoption of different preparations of tetanus toxoid by the two divisions of our forces reflects the diversity of opinion that prevails among immunologists concerning the relative merits of the plain or liquid and alum-precipitated toxoids. Certain persons in the Army prefer the former in the belief that its sensitizing properties are less than those of the alum-precipitated material and that it causes fewer reactions. There is no conclusive evidence that this is so, and certainly the convenience of administering only two doses of the precipitated toxoid is a definite advantage.

Yellow Fever

For a time, vaccination against yellow fever was required for all personnel in both the Army and Navy. Now, however, the Army has restricted its use to those about to depart for areas in which the disease is endemic. The vaccine developed by Theiler and Smith⁹ of the International Health Board at the Rockefeller Foundation consists of the living virus of yellow fever attenuated in virulence by prolonged passage in chick-embryo tissue cultures. At present, such a virus, propagated in the developing hen's egg, is employed for vaccination. One dose of 0.5 cc. of the concentrated virus-containing material, diluted 1:10 with sterile physiologic solution, is injected subcutaneously. Immunity results within a period of seven to ten days and lasts for at least three or four years and probably much longer. In perhaps 5 per cent of those inoculated, mild febrile reactions may be expected from the fifth to the seventh day following vaccination. Yellow-fever vaccine should not be given at the same time as smallpox vaccine, and an interval of at least five days must elapse before the latter is applied. There is no contraindication,

however, to simultaneous vaccination against yellow fever, tetanus and the enteric diseases.

Since the attenuated virus is extremely labile and readily becomes inactivated at ordinary temperatures, great care must always be taken to keep the vaccine at a temperature not higher than 4°C. Any diluted vaccine that has stood longer than three hours at room temperature must be discarded.

The vaccine in recent years has been administered without serious consequences to over 2,000,000 persons in South America and elsewhere under the supervision of the Rockefeller Foundation.

Cholera and Plague

In special instances, cholera and plague vaccines are used. Troops or naval forces about to enter areas where cholera is endemic or epidemic or where there is a serious threat of exposure to bubonic plague are given the appropriate vaccine. The cholera vaccine consists of 8,000,000,000 killed vibrios per cubic centimeter. The organisms are derived from a recently isolated strain, which should tend to ensure good immunizing properties. The suspension is injected subcutaneously in doses of 0.5 and 1 cc at an interval of seven to ten days. In contrast, the plague vaccine available, at least until recently, is made from old stock strains, and accordingly, its antigenic potency is open to considerable question. Until we have a better preparation, this material, which contains 2,000,000,000 organisms per cubic centimeter, is being employed and is administered in the same manner as the cholera vaccine. Up to the middle of last February, the Army had received no reports of untoward reactions following the injection of either preparation.

Everyone is aware that the efficacy of these vaccines is still in doubt. Although the experience of the British and East Indians with cholera vaccination and that of the Plague Commission with prophylaxis against plague in India strongly suggest that such procedures tend to decrease the incidence of both diseases, as well as to lower the mortality, it is as yet impossible to place as much confidence in them as we do in smallpox vaccination and the others that I have mentioned. Research by certain groups in this country with the object of obtaining better products is being actively pursued.

Typhus

Some allusion, perhaps, to vaccination against typhus fever of the classic or European variety is

appropriate. The prospect of the entrance of our forces into regions where this disease is endemic or epidemic makes vaccination highly desirable. A suitable preparation was believed to be at hand in the Cox¹⁰ yolk-sac vaccine. This, indeed, was used for a time in the Army and Navy. Tests, however, of its effectiveness as an antibody stimulant were disappointing, and its use has been discontinued. Vaccines prepared by different techniques, however, are available and are under investigation. Of these I shall mention only one, since I have firsthand knowledge of it.

This vaccine, devised in the bacteriological laboratory at the Harvard Medical School, consists of a suspension of killed rickettsias of the European type. The organisms are obtained from mice whose resistance to infection has been reduced by preliminary heavy exposure to x-rays. Experiments with guinea pigs and cotton rats have indicated that the material induces satisfactory immunity. Moreover, the serums of a small group of human beings, drawn from two to six weeks after a series of injections, have been shown to contain considerable amounts of antibody, which is capable of protecting both guinea pigs and cotton rats against a number of infecting doses of living rickettsias. The disadvantage of the method for large-scale production lies in the necessity of using the x-ray treatment and many thousands of mice. Should it be found desirable, however, to produce vaccine in this manner, I believe means could be found to circumvent such practical difficulties.

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WORLD CONFLICT AND MEDICAL SERVICE*

JOHN M. PRATT †

CHICAGO

WE are at war! Slowly, it is seeping into our consciousness that it is a new kind of war in a new kind of world; that it is of such scope and of such proportions that no single human intellect can comprehend—even remotely—its final implications.

We shall win this war. It may be months long or years long, but, ultimately, the eternal verities for which we wage war will emerge triumphant. There are in prospect months, many months, of toil such as we have never known; sacrifice such as we have never imagined—tears and sweat and blood and heartbreak.

There can be no question concerning the deadliness of the peril or the necessity for unlimited sacrifice and undivided devotion. American medicine is trained in service—it is now steeling itself to its part of the gigantic task that lies ahead.

In October, 1941, the Procurement and Assignment Service was formally authorized as a governmental agency. The mechanisms and functioning of this vital, all-professional agency, headed by Dr. Frank H. Lahey, a distinguished member of your society, have been fully explained. Suffice it for me to say that physicians are beginning to understand that to meet the developing necessity every doctor and every medical student will be called on to contribute to the extent of maximum individual capacity. American medicine will make—already is making—its vital contribution without question—without qualification—without reservation.

Two phases or aspects of the operation of the Procurement and Assignment Service, however, should receive special consideration. A comparison should be made. Day by day, as moves were made to convert our production facilities, our resources, our manpower to make them available for an all-inclusive, all-out effort for total war, it became progressively more essential to establish arbitrary and effective controls. Our automobile industry has ceased to exist. Tires are not purchasable. We are becoming accustomed to cuffless trousers and rubberless girdles. Sugar is rationed. And it is fully understood that these are merely the beginnings of the establishment of controls that, eventually and quickly, will apply to all essential supplies. Each processor of goods

in the United States must secure his raw materials through a constantly tightening system of priorities. He is told what materials he can have, how much of them can be provided, how they must be utilized and what disposition shall be made of the finished product. There is no complaint. It is accepted that such steps and such controls are essential to the effort that must be made.

This is the significant and truly important fact. In this country we have now progressed to the point where the medical, dental and veterinarian professions—under the Procurement and Assignment Service—are the only nation-wide groups that operate on the basis of self-administration and self-discipline. In all likelihood, the establishment of this service on such a basis is the greatest achievement of and the greatest tribute ever accorded to these professions in the United States. It should be accepted on this basis—and physicians should see that their portion of it functions with such effectiveness that compulsory controls are rendered unnecessary.

That is the first phase. Organized medicine is one of three nation-wide groups—vital to the war effort—that have retained their autonomy, which is self-administering and self-disciplining.

The second phase is that of the elements of danger involved. Almost without exception, the leaders of medical organizations—the trustees of the American Medical Association, the members of the House of Delegates and the presidents, secretaries and other officers of state medical societies—make up the organization that carries on the all-important task of the procurement and assignment of physicians. It is expected that 40,000, possibly 50,000 physicians will be called to serve with the armed forces.

For a quarter of a century, to an ever-increasing degree, American medicine has been conscious of the threat of so-called “socialized medicine”—more accurately defined as state medicine or the political control of medical practice. It must be kept in mind that, if the war continues two or more years, with ever-deepening intensity, with a constantly accumulating need for devotion and sacrifice, which is to be expected, we shall have established the machinery and possibly may have developed the habit of providing for the distribution of medical care through an agency of government.

Under these conditions, medicine must remember—must be made to remember—the funda-

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†Executive administrator, National Physicians Committee for the Extension of Medical Service.

mental factors that are responsible for its present place of pre-eminence. Its scientific achievement, its technical effectiveness, its capacity to anticipate this great emergency need, its ability to make the contribution it has made and will make in war effort are the result of conditions and principles under which it has been permitted to function.

The basic tenet of American medicine has been that where there was disease a life was the issue. It mattered not whether prince or pauper was involved. If we are to make progress, this principle must be preserved and sanctified. The whole of men's concepts are in flux. This basic tenet may be lost or sacrificed unless we make a task of preserving it. This is the first part of an essential wartime task of the medical profession. It in no way militates against or in any way detracts from our contribution toward winning the war. It is of the most vital importance if we are to preserve the form and pattern of medical practice and the independence of the profession.

There is a second part to this really grave responsibility of the medical profession. It is of equal, possibly of greater, necessity that the general public be kept conscious of the general superiority of American medicine and of the greater relative effectiveness of our system of distribution of medical care.

In a very real sense, this is a function of the National Physicians' Committee for the Extension of Medical Service. It is my hope that I may leave with you a definite and lasting understanding of the "why" and the method of functioning of this all physician organization—the National Physicians' Committee. In the short time allotted, in all likelihood, this can be done most effectively by illustration. As a case in point—each week, every week, an editorial service is provided for more than twelve thousand weekly newspapers throughout the United States. Keep in mind that it is essential that the public understand what it—the public—has to gain or lose by substituting a political control of medical care for our system of independent medicine.

Always these editorials deal with health matters of current interest. The following are typical titles. "No Mass-Production Doctors"; "Science Must Know"; "The Eternal War"; "The War Against Disease"; "Socialism Doesn't Insure Health"; "Science and Freedom." Each editorial has a short, final paragraph dealing with the relative effectiveness of American medical service and our system of the distribution of medical care. For example: "The doctor is a soldier—a soldier fighting an everlasting war against disease and plague and death. Today medicine is mobilized to make

that fight even more effective." Another last paragraph: "Private medicine has made strides that can be best described as miraculous in controlling and eliminating the great bacterial killers. The final result is twofold—longer lives for the people and happier, fuller lives as well." Another: "We Americans have more doctors and better doctors than any other nation. We Americans, rich or poor, receive in sickness far finer care than any other human beings. That is the way the system of private medicine proves its soundness—by its final results." Another: "In this country, the level of public health is the highest ever attained in the civilized world. But even that great achievement doesn't satisfy the medical men. They mean to achieve far more in the years to come. That is the way the medical mind works. It never stands still. It must always look forward." One more last paragraph: "American doctors oppose political tinkering in the field of medicine which would in all probability make for retrogression, not progress, in medical science."

To illustrate more concretely the purpose and the method, on February 4, 1942,—note this date, approximately two months after the treacherous attack on Pearl Harbor,—the Council of the Massachusetts Medical Society unanimously adopted a vitally important resolution in connection with proposed amendments to the Social Security Act. In part, the resolution reads:

WHEREAS, It seems to be the intent of this legislation to finance this extension, in the case of the employed, by a tax of 1 per cent on payrolls, one half of which is to be paid by the employer and one half as a deduction from wages,

WHEREAS, The people of these United States are now heavily burdened and will be further burdened by our war effort,

WHEREAS, This is the first step in the direction of the complete control of the care of the sick by Government, and,

WHEREAS, Wherever such control has existed the quality of medical care has suffered, therefore, be it

RESOLVED, That the Council of the Massachusetts Medical Society in regular session, February 4, 1942, does hereby oppose any such extension of the present Social Security Law as is herein outlined.

In connection with these same legislative proposals, the March 7 issue of the *Journal of the American Medical Association* carried a 2500 word editorial. I quote one short paragraph:

The American people are not averse to immense sacrifice—even to the ultimate sacrifice—if it will win the war. They should not be compelled, in the midst of such sacrifice, to consider radical proposals for changing the whole system of American living in health or in illness. The proposed expansions of the Social Security Act related to medical care should be considered in times when they can be given this type of

deliberate, meticulous consideration which carefully weighs every aspect of the problem concerned. Such proposals should not be submitted to the Congress and to the people in a period fraught with anxiety as to whether or not the nation itself will survive.

In this manner, clearly defined policy was established.

On March 23, the National Physicians' Committee provided its more than twelve thousand newspapers — with an estimated forty million readers — with an editorial, entitled "No Time for Wasteful Debate." It stated, in part, "It has been proposed that the Social Security laws be broadened in order to establish what would amount to a nation-wide system of compulsory sickness insurance." It quotes the above paragraph from the *Journal of the American Medical Association* and closes with this sentence, "This is certainly no time for debating a proposal which would take us a long way toward regimented, Europeanized, politically-dominated medicine."

On March 30, a second editorial, entitled "Not the Time," was provided for these forty million potential readers. The first and last two sentences of the editorial were as follows: "A definite campaign is underway to extend the Social Security Act to an extent never intimated when it was passed — and to an extent which would work a revolutionary change in American life." "This is not the time to dislocate a system of medical care which has produced such fine results. This is not the time to distract the attention of the people and the Congress with proposals which have no bearing on the incredibly difficult job of winning a war which comes ever closer to our own territorial borders."

On April 6, a third editorial was published. I quote the opening and concluding sentences: "While war news grips the headlines and the attention of the people, a movement is underway that would regiment the practice of medicine in this country." "This is not the time to debate a measure which would tend to make medical care a definite province of centralized government."

There was one more step in this systematic, continuing process. On March 24, the National Physicians' Committee was accorded the facilities of the approximately sixty radio stations comprising the Mutual Network for a fifteen-minute nation-wide broadcast. I quote from this broadcast:

American medicine believes that, at this time, there dare not be a division of effort. American medicine believes — and demonstrates its belief with deeds — that the war effort must be prosecuted with an unswerving singleness of purpose that will leave nothing to chance.

Now, unfortunately, there has been forced into this truly perilous situation legislative proposals which, if enacted into law, will take the first steps toward nul-

lifying the most sacred and basic concepts of the medical profession. Medicine, for itself, seeks nothing. Medicine asks for nothing save the preservation of conditions which enable physicians to apply their science and their skills to the best possible advantage. In the settlement of this grave issue the public has much to gain — with the alternative, the prospect of irreparable loss.

The broadcast quotes President Roosevelt on medical policy; it quotes the editorial in the *Journal of the American Medical Association*; and it concludes:

Eventually, after the war is won and the final victory is a reality, this vital issue can be reconsidered. If eventually some form of compulsory health or hospital insurance results — American physicians will accept the decision with a foreknowledge of its hampering, stultifying effect. For the time being, American physicians believe that there is one issue — now — winning the war.

This issue has been raised and must be met. It is not a matter of any selfish interest of the physicians of the United States. In a literal sense it is a matter of life and death. It directly affects one hundred and thirty million people who tomorrow or next week may be stricken with disease. At any cost, compulsion — any compulsion — should be avoided in the relationship between the patient and his physician. Tomorrow you may lunch with a friend — talk to him or her about this issue. You are a member of a club — make compulsory insurance the subject matter of discussion. Do this and you will do much — the one desire of American medicine is that the issue be really understood.

These circumstances have provided an opportunity for a concrete demonstration of the functioning of the National Physicians' Committee. There will be irreparable loss — if we fail to keep constantly in mind the fact that in the final analysis, *the public's opinion of the quality and effectiveness of medical service will become the deciding factor in the settlement of the problem.* They cannot know what it is, how it works, and of its relative effectiveness unless they are told. It has become definitely the responsibility of medicine to keep the public informed. In this instance, it was possible for the National Physicians' Committee to take the policy decision of the Council of your society and make it available to more than twelve thousand newspapers with nearly forty million readers and to carry the same message to hundreds of thousands, possibly millions, of radio listeners.

The first paragraph of the first document (*The Achilles' Heel of American Medicine*) ever published by the National Physicians' Committee reads:

The weak spot in American Medicine is in its singleness of purpose. Its greatest danger lies in the exclusiveness of its devotion to scientific improvement and technical effectiveness.

Under conditions now prevailing, the urge to the "limit of capacity service" is irresistible. Today,

American Medicine's greatest danger lies in the possibility of refusing or failing to keep in mind medicine's fundamental concepts during a period of abnormal crisis.

On this basis, the importance of the activities of the National Physicians' Committee has been multiplied greatly. Physicians must be made to keep in mind the fundamental factors responsible for its past achievements and its present unequalled effectiveness. The public—one hundred and thirty million people—must be kept aware of the fact that through our system of private medicine they have been the beneficiaries of the most effective and most widely and evenly distributed medical care that has ever been provided anywhere at any time. During the period of this greatest emergency, this is the primary function of the National Physicians' Committee.

During recent weeks,—since Pearl Harbor,—strong supporting committees have been organized: in Chicago, through fifteen branch societies; in Altoona, Lancaster, Williamsport and Philadelphia, Pennsylvania; in New York City—the Bronx, Richmond and Brooklyn—and in Buffalo, Rochester and Syracuse, New York. Many state societies have adopted resolutions providing for state-wide co-operation. It is hoped that with your commendation, the Council of your society may take official action in connection with approval of and support for the continuing work of the National Physicians' Committee, in order that during this trying period, when the necessity for controls is accepted and when regimentation is approved, we may be kept on the alert and constantly conscious of the elements of independence of action that are responsible for our past progress and our incomparable achievements.

Pittsfield Building

MASSIVE HEMATURIA OF RENAL ORIGIN*

GEORGE C. PRATHER, M.D.†

BOSTON

UNLESS one is aware of certain circumstances in medicine through personal experience or the experience of others, it is possible to arrive at false conclusions even when apparently sound reasoning has been used in formulating an opinion. As an example, profuse urinary-tract hemorrhages not infrequently occur from the necrotic or traumatized surface of a bladder tumor or from large, distended veins on the surface of an enlarged prostate; such hemorrhages are severe enough to fill and distend the bladder with blood and blood clot, and to cause acute urinary retention.

A hemorrhage of this magnitude from a renal lesion indicates that considerable blood has passed down the ureter to the bladder. If one remembers the physiology of renal and ureteral pain, the possibility for such a quantity of blood to pass down the ureter without causing renal pain owing to interference with drainage from the corresponding kidney seems rather remote. Yet the cases presented below demonstrate that renal bleeding sufficient to fill the bladder with blood and clots can occur without causing any discomfort in either kidney region.

In cases of severe urinary-tract hemorrhage without symptoms referable to the kidney region, there is always a temptation to open the bladder through a suprapubic incision, under the delusion that the

cause of the hemorrhage may well be found in the bladder or prostate. Knowledge that renal bleeding can produce an alarming collection of blood in the bladder without any symptomatic indication of the source of the hemorrhage should cancel this temptation, however, and should enjoin evacuation of the bladder through a rigid catheter, cystoscope or resectoscope, rather than by an exploratory incision. The endoscopic evacuation of the bladder should provide a medium sufficiently clear to permit observation of the ureteral jets or catheterization of both ureters, unless, of course, the source of the hemorrhage can be observed in the bladder or prostatic urethra.

The task of freeing the bladder of all clot is not always a brief or pleasant one. Not infrequently, an hour is spent in this procedure before a thoroughly satisfactory view of the bladder is obtained. For emptying the bladder of clot and blood in the circumstances under discussion, I have employed the sheath of either a No. 24 Fr. cystoscope or a resectoscope. Either the Ellik evacuator or a Janet type of syringe (glass barrel with steel plunger) can be attached to the distal end of these sheaths for alternate irrigation and suction. With the help of preliminary narcosis and local anesthesia, most patients can be handled without spinal or general anesthesia, although I see no objection to anesthesia for the procedure if the patient does not tolerate the maneuver with local medication.

*From the Urological Department, Boston City Hospital.

†Instructor in genitourinary surgery, Harvard Medical School; visiting surgeon for urology, Boston City Hospital.

After the bladder has been freed of its bloody content, cystoscopic observation usually reveals a bladder mucosa that is dull red, light absorbing, and lacking in normal luster. Following the inspection of the bladder itself for evidence of tumor, ulceration or other disease, it is advisable to watch the contractions of the ureteral orifices before they are catheterized. With severe bleeding from one kidney, careful observation of the ureteral orifices should disclose which kidney is at fault before the ureteral catheters are inserted. With this knowledge before catheterization of the ureters, the uncertainty of whether bloody urine draining from the ureteral catheter is due to true renal disease or the trauma of insertion is avoided. Catheterization of both ureters is desirable not only to provide pyelographic data of the bleeding kidney but also to demonstrate the integrity of the opposite one, should immediate removal of the diseased organ be deemed necessary.

Correct interpretation of the pyelogram of a bleeding kidney is notoriously difficult because of filling defects, which may be due to a blood clot in the kidney. However, the information obtained at the time of the emergency cystoscopy is essential either for a prompt diagnosis or for comparison with pyelographic data that might be obtained at a later date.

The immediate treatment naturally depends on whether prompt surgery seems to be necessary as a lifesaving measure to stop the hemorrhage or whether, after the bleeding has ceased, operation may be postponed until the problem has had further study and consideration. The general condition of the patient, the probable diagnosis and the state of the opposite kidney determine the appropriate treatment.

CASE REPORTS

CASE 1. W. G. (B.C.H. 983942), a 30-year-old man, was first admitted to the hospital on March 30, 1940, because of gross hematuria of a month's duration. Four days before admission, the hematuria became severe, and the patient passed large blood clots in the urine. There had been no pain in the kidney regions, but he described discomfort in the lower abdomen.

The past history was not significant, but the family history indicated exposure to tuberculosis in the household.

Physical examination disclosed no gross abnormalities except for the abdominal findings, which were those of a distended, tense bladder easily visible and palpable. The upper border of the bladder was at the level of the umbilicus. The whole lower abdomen was tender to palpation.

Laboratory data showed a red-cell count of 4,480,000 with a hemoglobin of 100 per cent, and a white-cell count of 8300. The nonprotein nitrogen was reported as 32 mg. per 100 cc. of blood.

An x-ray film of the chest was negative for tuberculosis.

Shortly after admission, the patient was catheterized, and the bladder evacuated of grossly bloody urine with a moderate number of clots. He was left on constant

drainage, and the hematuria disappeared spontaneously during the following 48 hours.

On April 5, cystoscopic study showed the left side of the bladder to be edematous, in addition to a small ulcer in that region. The mucous membrane of the remaining portions of the bladder revealed diffuse inflammation. The left ureteral orifice was deformed by edema and inflammatory changes. Both ureters were catheterized for



FIGURE 1. Intravenous Pyelogram.

There is an ulcerative lesion of the middle calyx of the left kidney. The lower left ureter shows an irregular dilatation.

specimens, and indigo carmine appeared from both ureteral catheters in 2½ minutes following intravenous injection. Intravenous pyelograms were obtained (Fig. 1).

A provisional diagnosis of left renal tuberculosis was made, and the patient was discharged from the hospital on April 10, pending report of guinea-pig studies of the kidney specimens.

The patient was readmitted on May 20, following autopsy of the inoculated guinea pigs, which indicated that the left kidney was positive for tuberculosis. On May 24, left nephrectomy was done through a lumbar incision. The kidney was easily exposed and delivered, and the ureter was ligated, bisected and tied approximately 10 cm. below the kidney pelvis. The pedicle was clamped, the kidney was removed, and the pedicle was securely tied. The wound was closed with a Penrose drain to the renal fossa. Convalescence was uneventful.

The pathological report described the weight of the left kidney as 120 gm.; several small, yellowish areas were scattered throughout the pyramids, pelvic mucosa and calyces. The microscopic diagnosis was tuberculosis of the kidney (Fig. 2).

On follow-up examination 1 year later, the wound was well healed, and the patient in good health.

CASE 2. J. D. (B.C.H. 967915), a 64-year-old man, was first admitted to the hospital on January 11, 1940, for acute urinary retention and gross hematuria. He had experienced urinary retention twice, but each time had resumed voiding after catheterization. He had recently passed grossly bloody urine and clots, but he had been unable to void for several hours prior to admission. At no time did the patient have any pain in the kidney regions.

Physical examination disclosed no pertinent physical findings except a distended bladder easily visible and palpable in the lower abdomen. There was no mass or tenderness in either kidney region. On rectal examination, the prostate showed benign enlargement.

Laboratory studies disclosed a red-cell count of 2,600,000 with a hemoglobin of 50 per cent and a white-cell count of 16,400. The nonprotein nitrogen was reported as 35 mg per 100 cc. of blood.

The patient was catheterized and placed on constant urethral drainage. Grossly bloody urine, with clots, was

On January 20, a suprapubic cystostomy disclosed a very large blood clot and foul urine in the bladder. Intravesical enlargement of the prostate was observed, but no bladder tumor could be identified. A suprapubic tube was placed in the bladder, and the wound closed. Following the operation, lack of improvement was evident. The patient became septic, his general condition declined, and he



FIGURE 2. Tuberculous of the Kidney.

This low-power photomicrograph of a section of the left kidney shows a large area of caseous necrosis, with tuberculous granulation tissue on the periphery.

obtained. On drainage, the urine remained somewhat bloody. Cystoscopy on January 14, 3 days after admission, still showed a quantity of bloody urine in the bladder, which was evacuated through the cystoscope. When a fairly clear medium could be established, it was thought that the patient probably had a malignant tumor on the posterior bladder wall, which obscured satisfactory vision of the bladder base and trigone. Neither ureter was catheterized, and no pyelographic studies were done. Following this examination, hematuria did not cease, and the patient's general condition was only slightly improved by two blood transfusions.



FIGURE 3. Bilateral Retrograde Pyelogram.

The lower calyx of the right kidney is shortened and partially obliterated.

expired about 6 weeks after operation. There is no indication on the record concerning whether or not the drainage remained clear.

At autopsy, the right kidney weighed 500 gm, and on microscopic section the upper pole was occupied by a tumor measuring 60 by 100 by 6.5 cm.; the grey red tumor extended into the pelvis and obstructed the ureter at its origin. More of the tumor could be seen in the veins and arteries of the kidney. The bladder mucosa was of increased thickness and red grey, but no tumor of the bladder could be demonstrated. The diagnosis was carcinoma of the right kidney.

CASE 3. M. C. (B.C.H. 978178), a 38-year-old man, was admitted to the hospital on April 6, 1940, with the diagnosis of acute urinary retention and gross hematuria. His general health had been good. The patient had experienced no urinary symptoms until 24 hours before admission, when he noticed blood in the urine. The hematuria continued with the passage of some clots. A few hours before admission, he was unable to pass any urine. His physician was called, but since an attempt at catheterization failed, the patient was referred to the hospital. There had been no complaint of pain in either kidney region.

Physical examination disclosed no pertinent findings except for examination of the abdomen, where a distended

bladder was easily visible and palpable. There was no tenderness or enlargement in either kidney region.

Laboratory studies revealed a red-cell count of 4,700,000 with a hemoglobin of 80 per cent, and a white-cell count of 12,300. The nonprotein nitrogen was reported as 23 mg. per 100 cc. of blood.

The patient was catheterized easily with a soft catheter, bloody urine and a blood clot from the bladder being evacuated.

Cystoscopy 2 days later showed the bladder mucosa to be red and edematous. Both ureteral orifices were



FIGURE 4. *Right Retrograde Pyelogram.*

The filling defect in the upper right ureter is due to blood clot. The lower calyx of the right kidney is distorted.

edematous, and dark urine could be seen coming from the left ureteral orifice. On the left lateral wall of the bladder, a small ulcer was visible. Both ureters were catheterized, specimens were obtained from each kidney, and a retrograde pyelogram was done. The pyelographic report indicated a filling defect 2.5 cm. in diameter involving the renal pelvis and superior calyx; this was thought to be tumor rather than blood clot.

On April 16, a left nephrectomy was performed through a left lumbar incision. The upper pole of the kidney was irregular and cystic to touch.

Pathological study of the removed kidney showed one entire pole to be cystic. In addition, there were five small, yellow nodules protruding from separate areas on the surface of the renal cortex. The microscopic diagnosis of the removed kidney was renal tuberculosis and chronic pyelonephritis.

Convalescence was uneventful, and the patient was discharged to a sanatorium on May 4. He was discharged from the sanatorium in good condition approximately 6 months later.

CASE 4. F. D. (private patient), a 64-year-old man, was admitted to a hospital on February 20, 1941, because of gross hematuria, which had begun 2 days previously. Several hours after he first noticed hematuria, it became difficult for him to pass any urine. His physician catheterized him, irrigated the bladder free of clot, and sent him to the hospital. At no time had the patient noticed discomfort in either kidney region. On arrival, he was comfortable and voided amber-colored urine easily.

The past-history was irrelevant.

Physical examination disclosed no gross abnormalities. The blood pressure was 140/82. Abdominal palpation revealed no mass or tenderness. The bladder was not palpable or percussible. The external genitalia were nor-

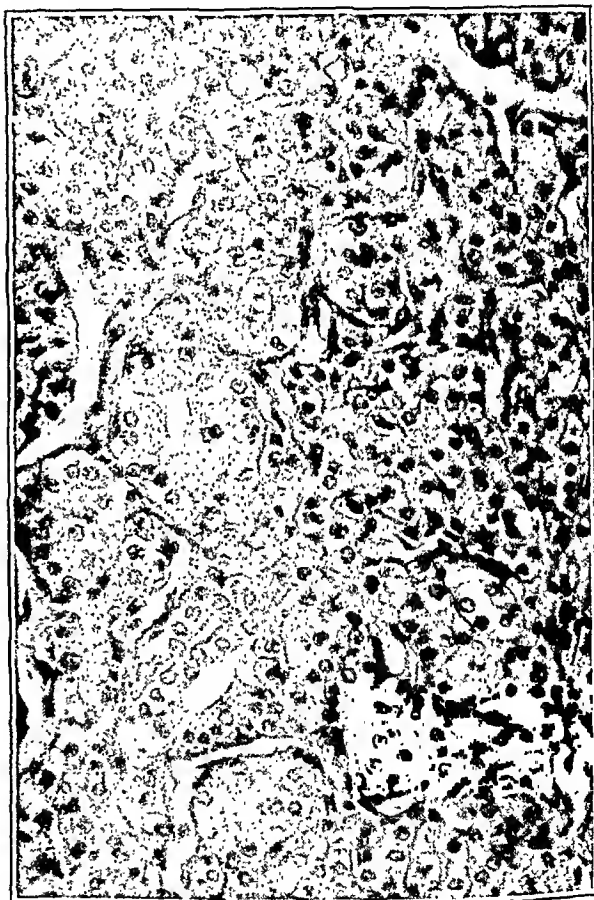


FIGURE 5. *Renal-Cell Carcinoma.*

This section through the more compact portion of the tumor in the right kidney shows the tubular arrangement of the cells with only a moderate degree of vacuolization. The scantiness of the stroma is marked.

mal, and by rectal examination the prostate was normal in size and consistence.

Cystoscopy and a pyelogram were done the day following admission. The bladder appeared normal in all respects. No intravesical enlargement of the prostate was

noted, both ureters were catheterized easily, and clear urine drained from both kidneys. Good function of both kidneys was demonstrated by intravenous phenolsulfone phthalein. A bilateral pyelogram was taken. The pyelographic report failed to describe any dilatation or abnormality of the kidney pelvis or ureters (Fig 3).

Following cystoscopy, the patient voided clear urine for 36 hours, and suddenly he passed a large quantity of blood and blood clot through the urethra. Within 1 hour the bladder became distended with blood clot. At cystoscopy over 700 cc of blood and bloody urine was removed from the bladder by suction and irrigation through the cystoscope. After thorough washing of the bladder it was possible to visualize a long, stringy blood clot protruding from the right ureteral orifice. The right ureter was catheterized without difficulty, and a pyelogram made (Fig 4). This second pyelogram of the right kidney showed an apparent enlargement of the lower pole of the kidney that had the appearance of tumor.

On February 23 immediately after cystoscopy, a right nephrectomy was performed under spinal anesthesia through a right flank incision. The kidney contained a large, solid tumor at its lower pole. Intravenous glucose and a blood transfusion were given at the conclusion of the operation.

The pathological report of the excised kidney disclosed primary carcinoma of the kidney (Fig 5).

Convalescence was uneventful and the patient was discharged from the hospital on March 14.

Following discharge, he had a program of deep external radiation, which was completed on June 20. So far his

health has remained good and there has been no clinical evidence of recurrence of tumor either in the wound or at distant points.

Cases 1, 3 and 4 illustrate what is, I believe, the proper handling of the problems they present. Case 2 shows clearly the error that can easily be made—that is, interpreting blood clot in the bladder as evidence of bladder disease and proceeding with bladder surgery when the cause of the bleeding is a renal lesion.

CONCLUSIONS

Bleeding sufficient to fill the bladder with clots and cause acute urinary retention may be due to a renal lesion. The passage of a large quantity of blood from the kidney to the bladder can occur without causing discomfort in the kidney region or giving any clinical symptoms indicative of the source of bleeding.

If errors in treatment are to be avoided, careful evacuation of clot by endoscopic means must be done, and the source of the bleeding must be demonstrated. Occasionally, prompt nephrectomy is necessary as a lifesaving measure to avoid fatal hemorrhage.

99 Commonwealth Avenue

CLINICAL NOTE

DETERIORATION OF MILK BY BACTERIAL GROWTH UNDER REFRIGERATION AT 40°F.*

FRANK E. MOTT † AND HENRY MAZER ‡
BOSTON

IN consideration of the possible effect of the adoption of delivery of milk every other day by dealers in Metropolitan Boston, it appeared desirable to ascertain what the change in the bacterial content of milk might be from day to day in a modern refrigerator at 40°F.

Such a study was undertaken, and the original in-

of bacteria from 1 cc. that their sale would be in violation of the law and standards of the Commonwealth of Massachusetts, which have been adopted for the protection of public health.

Certified milk-pasteurized, on the other hand, even after ninety-six hours in the refrigerator, still conformed to the bacterial standards and was perfectly safe for use as measured by present knowledge of the subject. After four days in the refrigerator at 40°F., both Grade A milk-pasteurized and Grade B milk-pasteurized had bacterial contents so great that their use might reasonably be expected to cause diarrhea and enteritis in children under six years of age.

To estimate the effect on bacterial growth of shutting off the refrigerator and the ensuing gradual rise in temperature, in one group of experi-

TABLE 1. Growth of Colonies of Bacteria from a Cubic Centimeter of Milk.

TYPE OF MILK	No. OF SAMPLES		No. OF COLONIES					
			ON DELIVERY	1 DAY AT 40°F.	2 DAYS AT 40°F.	3 DAYS AT 40°F.	4 DAYS AT 40°F.	5 DAYS AT 40°F.
Certified-pasteurized	22	Maximum	20	40	100	850	1,000	1,400
		Minimum	0	4	5	8	15	20
		Average	8	14	44	157	286	770
Grade A-pasteurized	12	Maximum	700	4,000	20,000	200,000	650,000	5,500,000
		Minimum	100	150	200	300	2,000	5,000
		Average	300	1,300	4,300	110,000	190,000	1,300,000
Grade B-pasteurized	12	Maximum	15,000	26,000	65,000	130,000	500,000	8,000,000
		Minimum	2,000	2,000	2,000	3,000	4,000	20,000
		Average	6,000	9,600	15,000	41,000	130,000	1,700,000

vestigation included Grade A milk-pasteurized, commonly called "Grade A milk," and Grade B milk-pasteurized, commonly called "milk-pasteurized." At the request of the Medical Milk Commission of Boston, Incorporated, the investigation was enlarged to include certified milk-pasteurized, produced under the supervision of the commission. The samples of milk were obtained from vehicles on the streets of Boston engaged in the delivery of milk during the period, March 3 to May 10, 1942. Table 1 shows the results of the study.

The colonies of bacteria were counted by the standard plate method of the American Public Health Association, with the plates incubated at 32°C.; the numbers listed are the arithmetical averages, which were used purposely so that the important effect of the lack of uniformity might not be lost.

After seventy-two hours in the refrigerator at 40°F., both Grade A milk-pasteurized and Grade B milk-pasteurized had such a growth of colonies

ments the refrigerator was turned off at the end of the second day, and samples of milk were taken then and at the end of the third day, when the temperature had risen to 53°C. The results are presented in Table 2.

Both Grade A milk-pasteurized and Grade B milk-pasteurized had undergone such an increase in bacterial growth that their use might have caused diarrhea and enteritis in young children.

TABLE 2. Growth of Colonies of Bacteria from a Cubic Centimeter of Milk before and after Stopping Refrigeration.

KIND OF MILK	AVERAGE NO. OF COLONIES	
	AFTER 2 DAYS AT 40°C.	1 DAY LATER (53°C.)
Certified-pasteurized	100	300
Grade A-pasteurized	5,000	540,000
Grade B-pasteurized	10,000	100,000

But certified milk-pasteurized conformed to the bacterial standards adopted for that grade of milk, and was still perfectly safe to use as measured by present standards.

In view of these findings, it is evident that the present conception of the inhibiting effect of refrigeration on bacterial growth in milk must be revised.

*From the Milk Inspection Service, Boston Health Department.
†Chief chemist and inspector of milk, and director of the Laboratory for Chemistry and Sanitary Biology, Boston Health Department.
‡Assistant chemist and sanitary biologist, Boston Health Department.

MEDICAL PROGRESS

DIABETES MELLITUS

ELLIOTT P. JOSLIN, M.D,* and HOWARD F. ROOT, M.D†

BOSTON

STATISTICS

FOR 1939, the death rate for diabetes in the registration area of continental United States was 25.5 per 100,000, but in 1940 it rose to 26.6, with 35,015 deaths, the highest figures yet recorded. In 1941, however, there are indications from various sources that this upward rise is reaching a peak and that the deaths from diabetes have begun to decline from the previous rate. Thus, among the 17,000,000 industrial policyholders of the Metropolitan Life Insurance Company, the diabetic

physician, when he signs the death certificate, to minimize the importance of what is apparently the secondary cause of death—diabetes—or even omit it and register alone the actual cause, such as arteriosclerosis in its multiple manifestations, cancer, tuberculosis or similar but less frequent maladies.

The duration of life of diabetic patients is lengthening. The outcome of the first 10,000 patients (1898–1931) who consulted us on account of glycosuria has been investigated this year. The

TABLE 1 Survival after Onset in 6596 Fatal Cases of Diabetes*

AGE AT ONSET	NATALISM ERA		VINTAGE ERA		BANTING ERA		HYPERBURN ERA			
	— to	5/31/14	6 1/4 to	8 1/2 to 12/31/29	1/1/30 to	12/31/36	1/1/37 to	12/31/39	1/1/40 to	
	—		—		—		—		—	
yr	yr		yr		yr		yr		yr	
0-9	13		29		28		3		113	89
10-19	2		7		34				8	139
20-39	43		49		89		148		169	196
40-59	0		80		95		171		141	155
60 and over	44		64		55		12		8	103
Averages	49		61		81		107		125	143

*These figures were prepared by the Statistical Department of the Metropolitan Life Insurance Company; we are particularly indebted to Mr. Herbert H. Marks and Miss Edith Haldenstein.

mortality rate in 1940 was 29.5, and in 1941, 26.8 per 100,000. Similarly, drops, ranging up to 18 per cent, occurred in the reported rates for 1941 compared with those for 1940 in New York City (41.6 to 40.7), Chicago (38.0 to 31.1), Philadelphia (41.9 to 40.4), Boston (41.1 to 38.4) and Cincinnati (43.0 to 36.8).

The explanation of this decreasing mortality is at least threefold. In 1941, the good effects of the sulfonamide drugs became manifest in pneumonia and other infections—complications that have always taken a heavy toll of diabetic patients. Furthermore, the treatment of diabetes has steadily improved, largely owing to greater familiarity with the use of insulin and particularly to the protecting quality of protamine zinc insulin because of its prolonged action. Finally, this lengthening of life of the diabetic patient of itself, along with the better control of the disease, influences the

results, which have not hitherto been published, although they were cited in part at the meeting of the Association of American Physicians last May and formed part of an exhibit at the American Medical Association in June, are set forth in Table 1, in which for comparison are included data for earlier periods and also any deaths that were known among patients seen after 1931. These data are based on 6596 fatal cases that were seen up to and including April 20, 1942.

Fourteen and three tenths years now represents the average duration of life of recent fatal cases of diabetes seen one or more times in this clinic, in contrast to 4.9 years, which held before June 1, 1914. This figure deserves especial recognition because 30 per cent of the patients in 1940–1942 were already sixty years of age or older at the onset of their disease. With a gain of 3.6 years of life since the period, January 1, 1930, to December 31, 1936, based on fatal cases, it is reasonable to assume that the present expectancy of life in diabetes, as compared with that computed for our living and dead patients in 1938 by the Statistical Department of the Metropolitan Life Insurance Company, has risen from two thirds to nearly

Reprints of articles in this series are not available for distribution. But the articles will be published in book form. The current volume is *Medical Progress Annual Vol III 1941* (Springfield Illinois Charles C. Thomas Company 1941 \$5.00).

*Medical director, George F. Baker Clinic, New England Deaconess Hospital.

†Associate in medical clinic, Harvard Medical School physician, New England Deaconess Hospital.

three quarters that of the population as a whole, and we hope that the recomputations will prove this to be true. The significance of this trend on later possibilities of diabetic patients for employment or life insurance should not escape notice. The duration of life in diabetic children with onset of the disease under ten years of age is low. It should be stated, however, that since August 7, 1922, only 68 of these children have died and that 800 are known to be alive; it is obvious that the duration of the disease in the latter will eventually prolong the average of the group as a whole.

A survival of less than five years was the rule prior to August 7, 1914; in fact, it included 66.8 per cent of all cases, but this percentage has now dropped to 13.0 (Table 2). The percentage of

TABLE 2. *Survival in 6596 Fatal Cases after Onset of Diabetes.*

ERA	SURVIVAL	
	LESS THAN FIVE YEARS	TWENTY YEARS OR MORE
	%	%
Naunyn	66.8	1.8
Allen	55.9	3.1
Banting		
Early	40.5	4.0
Late	22.5	10.2
Hagedorn		
Early	15.0	14.4
Late	13.0	19.2

patients surviving twenty years or more has risen from 1.8 in the earlier era to 19.3 today; 8.2 per cent survived even twenty-five years of the disease. There are also known to be 73 children, 71 of whom are alive, whose onset of diabetes occurred when they were under fifteen years of age and whose subsequent duration of life has reached twenty years or more.

Deaths from diabetic coma have fallen from 63.8 per cent in the Naunyn Era (1898-1914) to 3.3 per cent since January 1, 1940. Moreover, of the last 62 successive cases (October, 1940, to July 24, 1942) of proved diabetic coma, with a carbon dioxide combining power of 20 vol. per cent or below, under our immediate care at the New England Deaconess Hospital, there have been no deaths, and 12 of these patients were unconscious. Diabetic gangrene, which caused 8.5 per cent of the 1448 deaths from 1922 to 1929, was the cause of 4.7 per cent among 929 deaths from 1937 to 1940, although the average age of the patients rose approximately 8.0 years and the duration of the diabetes from 8.1 to 12.5 years.

SEASONAL INFLUENCE ON DIABETES

The *mortality* from diabetes is greater in the winter than in the summer. Dr. Herbert L.

Lombard¹ proved this by computing the deaths from diabetes in the United States for a year, using the deaths from cancer as a control. Thus, in December to May inclusive, the deaths from diabetes were 16,926 and in June to November inclusive, 13,661, whereas the comparable but adjusted deaths from cancer were 15,294 and 15,293. On the other hand, season had no influence on the *onset* of the disease. For this purpose, the data were limited to the cases of children seen in our clinic; the onset in adults is uncertain whereas in children it can be somewhat more accurately assigned. The figures for the children during the winter and summer months for the different types of onset are as follows: onset indefinite, 270 in winter and 267 cases in summer; gradual, that is, within two months, 347 in winter and 336 in summer; rapid, that is, within seven days, 80 in winter and 89 in summer; and sudden, that is, in the course of twenty-four hours, 91 in winter and 91 in summer.

ROLE OF HYPERGLYCEMIA IN DEVELOPMENT OF DIABETES

Perhaps the greatest contribution to the treatment of diabetes during the last year is the demonstration by Lukens and Dohan,² of the George S. Cox Medical Research Institute, University of Pennsylvania, that, in cats, hyperglycemia precedes the degeneration of the islands of Langerhans and that, by overcoming it within a period of three months after the production of diabetes in this animal by injections of anterior pituitary extract, one can reverse the process in the islands and can cure the animal. Nothing has better supported the orthodox treatment of diabetes than Lukens and Dohan's experiments in the forty years since Naunyn wrote that the patient with early, but apparently severe, diabetes if treated energetically would eventually do quite well, whereas the mild case if neglected would progress unfavorably. In previous progress reports,^{3,4} reference was made to the work of these authors and to that of others, but we consider the following paragraph of repetition justifiable, because of the crucial importance of the subject from the human therapeutic point of view.

The sequence of events revealing the significant relation of the pituitary gland and diabetes brings to mind the work of Cushing and Davidoff,⁵ who observed that 12 per cent of 100 cases of acromegaly had diabetes and 25 per cent showed glycosuria; this figure was later raised by Coggeshall and Root,⁶ in a series of 153 cases placed at their disposal by Cushing, to 17 per cent and 36 per cent respectively. Houssay's⁷ epoch-making experiments showed that the removal of the pituitary gland lessened the severity of diabetes in the

depancreatized toad, and that injection of pituitary extract into such animals made the disease worse. Evans⁸ observed glycosuria following the injection of the extract of the anterior pituitary in dogs. Young⁹ produced out and out diabetes in 1 dog by repeated injections of anterior pituitary extract, with demonstrable destruction of the islands of Langerhans. Best and his collaborators¹⁰ confirmed Young's work and proved that if the injections of pituitary extract were accompanied simultaneously by injections of insulin,—or, as later shown, by fasting or a high fat diet,—the development of the diabetes was prevented. Finally, and contemporaneously with the work at the University of Toronto, Lukens and Dohlan² confirmed in 1 cat Young's original observation in 1 dog, but in the diabetically resistant cat it was necessary first of all to remove a portion of the pancreas, although not enough to cause glycosuria. These experiments emphasized the importance of hydropic degeneration of the beta cells as the pathologic state in the early stages of diabetes before atrophy, hyaline degeneration, fibrosis and lymphocytic infiltration occur. The studies of Lukens and Dohlan confirmed Allen's¹¹ observation that hydropic degeneration in the partially depancreatized dog is reversible by fasting, and also by the administration of insulin (Copp and Barclay¹²). In severe diabetes, this was accomplished with insulin, and in milder cases of the disease, by a reduction in diet and, finally, by lowering the blood sugar with phlorhizin.

In their article, which deserves detailed study because it summarizes the work of the authors mentioned above and a few others, Lukens and Dohlan² write

As a working hypothesis, the development of the permanent phase of diabetes may be stated as follows. The administration of pituitary extract results in (a) the production and maintenance of hyperglycemia, probably by its extra-pancreatic action, and (b) the damage to the pancreatic islands associated with this hyperglycemia, be it as cause or effect. A discussion of the possibility that injury to the islands may result from hyperglycemia must take account of two facts. These are the diminished liberation and content of insulin induced by pituitary extract and the increased production of insulin which follows elevation of the blood sugar in the normal animal. The results of Best, Campbell and Haist provide the most recent correlation between pancreatic insulin, blood sugar levels and island lesions. Regardless of the changes in insulin content, no permanent or irreversible damage to the islands has been produced by anterior pituitary treatment except when there is concomitant hyperglycemia. In addition, in the case of the cat, the high blood sugar persists after stopping pituitary extract even though the pancreatic lesions are still reversible. This suggests that hyperglycemia maintains the island damage (a vicious cycle). Stated in brief, the hypothesis that the elevation of the blood glucose is an important factor

in the causation of island pathology is supported by the following general observations: (a) Partial pancreatectomy or pituitary extract do *not* cause island lesions in the absence of hyperglycemia and (b) each leads to hydropic degeneration after hyperglycemia has been present for 1 week or two. (c) The elevation of the blood sugar by perfusion has resulted in early lesions of the islands. (d) The islands are restored by various types of treatment which return the blood sugar to normal levels.

These authors emphasize the need for an open mind concerning the pathogenesis of diabetes. This is because Long,¹³ in New Haven, and Ingle,¹⁴ in the Cox laboratory, found almost no hydropic change or atrophy of the islands in rats subjected to marked hyperglycemia for periods of from two weeks to several months, although such findings have been reported by Friedman and Marble.¹⁵

EXPLANATION OF TALL DIABETIC CHILD AND FAT DIABETIC ADULT

Young¹⁶ comments on the emphasis laid by our group¹⁷ on obesity in adults and overheight and precociousness in children as a prelude to the onset of diabetes. He cites our query—"In the child, growth is vertical, in the adult it is lateral. Is not each type of endocrinal origin?"—and proceeds to solve it in a series of experimental investigations, concluding "that a positive answer might be given to Joslin's question in terms of pancreatic hypophyseal balance."

Young refers to the first demonstration of the diabetogenic action of anterior pituitary extract in normal animals by Evans,⁸ in which two puppies treated daily with a growth promoting preparation of ov pituitary gland increased twice the weight of control animals and developed polyuria and glycosuria. The pituitary extract that Young used in the causation of diabetes in the adult dog was accompanied by a growth promoting substance. Others have also shown a similarity in properties between the growth promoting and diabetogenic substances. Young notes that Evans, for the growth hormone, and Houssay,⁷ for the diabetogenic substance, emphasized the value of using absolutely fresh glands and carrying out all procedures at low temperatures, and he therefore considers it surprising that more cases have not been recorded of the development of a diabetic condition in puppies in which gigantism has been produced by treatment with growth promoting pituitary extracts.

Recalling that, with the adult dog effectively treated with diabetogenic extract, eventually a refractory state developed, during which the symptoms of diabetes disappeared until the daily dose of extract was increased, Young points out the

possibility that the puppies treated with growth hormone did exhibit a transient response to the diabetogenic action of the extract but subsequently became refractory to it while retaining a sensitivity to its growth-promoting effect. In a series of experiments utilizing evidence, already furnished by Evans and by Mirsky,¹⁸ that growth-hormone preparations induce retention of nitrogen and that this nitrogen-retaining action may be mediated by the islands of Langerhans of the pancreas, he investigated the relation between the nitrogen-retaining and pancreatropic actions of anterior pituitary extracts in permanently diabetic animals in which some islet tissue remained.

Young observed that with normal cats and normal dogs an increase in body weight is associated with induction of a diabetic condition produced by the administration of crude pituitary extract, and he points out that Ogilvie¹⁹ presented quantitative evidence that human infants have a greater amount of pancreatic islet tissue in proportion to body weight than adults. Indeed, Langfeldt,²⁰ years ago, noted that partially depancreatized puppies, which had been deprived of a sufficient portion of pancreas to provide a reasonable expectation of the appearance of diabetes in an adult dog, not only were free from all symptoms of diabetes for many months after the operation but also, in some cases, showed an increase of sugar tolerance; however, the sugar tolerance eventually declined, and evidence of progressive and fatal diabetes became manifest.

Space does not allow presentation of Young's experiments in detail, but his own summary is as follows:

When puppies are treated daily with doses of crude pituitary extract greatly in excess of those required to produce diabetes in adult dogs, they respond with an increased growth rate but do not exhibit symptoms of diabetes. When one puppy was treated daily for nearly five months it eventually became intensely diabetic, and then stopped growing despite continuation of treatment.

When adult dogs that have been rendered permanently diabetic by a short period of pituitary treatment are given a single injection of pancreatropic pituitary extracts, which produces no detectable diabetogenic activity in normal adult dogs, the response may be a transitory attenuation of the diabetic condition with nitrogen retention and increase of body weight or an exacerbation of the diabetes with loss of nitrogen and of body weight; intermediate responses were also obtained. These differences in response are believed to result largely from differences in functional capacity of pancreatic islet tissue.

It is suggested that an increase in body weight, associated with an increase in function of the pancreatic islets, can be regarded as neutralizing, for a time at least, the diabetogenic influence of the anterior pituitary gland. It is therefore possible that the excessive weight of the adult diabetic patient and the abnormal height

of the diabetic child (White) indicate an increased pituitary function which may be of temporary duration only, and of which the diabetogenic action may be completely masked for a time by a protective increase in pancreatic islet activity, induced by the pancreatropic action of the gland. Such a condition might lead first to an increase in the mass of the body and eventually to diabetes.

INFLUENCE OF ESTROGENS AND ANDROGENS ON CARBOHYDRATE METABOLISM

The influence of the estrogens and androgens on carbohydrate metabolism in normal and diabetic animals continues to excite curiosity. Apparently, the effects observed in the intact animal are quite different from those in animals partially or wholly diabetic, and the results in human beings are rather difficult to interpret. Griffiths, Marks and Young,²¹ using normal rats in fasting condition, were able to show that the administration of estriol and estradiol, like that of diethylstilbestrol, promotes glycogen storage in the liver, whereas estrone and testosterone do not. Parallel increases in the amount of insulin in the pancreas also occur. Similarly, Fraenkel-Conrat et al.²² were able to produce increase in pancreatic insulin when prolonged estrinization of normal rats was carried out. They conclude that two types of evidence favor the assumption that the activity of estrogens in elevating the pancreatic insulin is due to the pituitary gland—namely, the pituitary glands of such rats, when implanted in other animals, elevate the pancreatic insulin content, whereas the glands of untreated rats do not show this activity. Moreover, estrogen, which raises the pancreatic insulin content in normal rats, does not have this effect in animals whose pituitary glands have been removed. On the other hand, when Ingle²³ administered stilbestrol to partially depancreatized rats on a constant medium-carbohydrate diet, severe glycosuria and hyperglycemia occurred in all cases. Similar results were obtained with dihydrostilbestrol, estradiol and equilin. Also, large doses of testosterone and methyl testosterone were weakly diabetogenic. In another series of studies, Ingle²⁴ showed that the administration of 17-hydroxy-11-dehydrocorticosterone to normal rats that were force fed with a high-carbohydrate diet caused hyperglycemia, glycosuria and an increased excretion of nonprotein nitrogen, with atrophy of the testes and thymus gland. These results seem to be confirmed by the experiments of Long,²⁵ which suggest that stilbestrol behaves somewhat like the adrenocortical hormone. In the studies by McCullagh,²⁶ the use of methyl testosterone in rabbits produced a low-carbohydrate tolerance, whereas testosterone propionate did not lower the carbohydrate tolerance. The favorable effects of methyl

testosterone in adult diabetic patients reported by some authors has not been confirmed by others.

In reporting the clinical use of stilbestrol in 79 diabetic women in the premenopausal, menopausal and postmenopausal years, Beardwood²⁷ was able to reduce the insulin dosage by an average of 11 units in 36 cases. In a group of 14 patients treated with large doses of Progynon B, an average reduction of 18.3 units in insulin dosage occurred in 8 patients. He concluded that estrogenic substances cannot be considered a substitute for the well established standard treatment of diabetes with diet and insulin, but that these special preparations had a stabilizing effect in a special group whose diabetes was very labile.

SPECIES DIFFERENCES IN DIABETES FOLLOWING PANCREATCTOMY

Species differences in diabetes following pancreatotomy have been emphasized by Mirsky.²⁸ The greatest rise in blood sugar is observed in cats, monkeys, man, owls, snakes, dogs and rabbits in decreasing order. Animals like the duck and the chicken, on the other hand, show almost no rise of blood sugar after pancreatotomy and, indeed, no increase in blood acetone. One might say, therefore, that human diabetes is a species diabetes differing in some respects from that observed in other animals.

RESISTANCE TO INSULIN AND ALLERGY

Resistance to insulin associated with allergy to insulin has been reported in a number of cases, but it may have greater significance than has yet been realized. It is possible that such frequent although not necessarily extreme cases of insulin resistance as occur during certain types of infection may be due really to manifestations of allergy. In 2 recent cases at the New England Deaconess Hospital, allergy to insulin was associated with insulin resistance and the occurrence of specific insulin precipitins in the blood. In one case, both asthma of long duration and an acute infection were present in a patient whose diabetes rapidly became so severe that actual, serious acidosis occurred. It is possible that the acute infection stirred up general antigenic manifestations in the body and that, as a result of this change, insulin resistance occurred. Lowell²⁹ reports studies on a forty-three year old woman who had severe urticaria following injections of crystalline and regular insulin. In this case, it was found that the patient was very resistant to ordinary crystalline insulin so that an injection of 30 units intravenously caused a slight rise in the blood sugar, followed by a fall to a point only slightly below the fasting level. On the other hand, when 30 units of insulin prepared from human pancreas were

injected intravenously, a fall in blood sugar took place so rapidly that a hypoglycemic reaction occurred at the end of ninety minutes, when the blood sugar was 59 mg per 100 cc in contrast with the fasting blood sugar of 330 mg. However, a marked allergic reaction, which was characterized by urticaria and constriction in the throat, occurred within fifteen minutes after injection of the human insulin. Tests with mice for insulin-neutralizing antibody showed that the patient's serum neutralized crystalline insulin, because the addition of serum to insulin when injected into the mice prevented a hypoglycemic reaction, such neutralization did not occur when human insulin was used. By a passive transfer test, it was shown that skin sensitizing antibodies were present in repeated specimens of the patient's serum over a period of six months. It was possible to sensitize normal skin to crystalline and human insulin by the injection of serum from the patient in dilutions varying from 1:16 to 1:64.

It is clear, therefore, that allergy to insulin can exist in the absence of resistance, and that resistance can exist in the absence of allergy. In Lowell's patient, resistance to crystalline insulin but not to human insulin was present. The patient reacted allergically to both crystalline and human insulin, and skin sensitizing antibody was present for both. The patient's serum, therefore, contained an antibody for insulin, which protected mice from a lethal dose of crystalline insulin but failed to protect against human insulin. It may be concluded that two antibodies were present in the patient's serum: an allergic antibody, which conferred sensitivity on normal skin, and an insulin neutralizing antibody, which was capable of destroying the physiologic effect of crystalline insulin.

Hyperinsulinism in a forty-year old man was treated successfully by Allen³⁰ with a diet high in carbohydrate in contrast to the diet sometimes recommended, in which a high protein content is used in the hope that a slow liberation of carbohydrate will counteract the hypoglycemia. The patient's weight was allowed to fall from 237 to 228 pounds. The blood sugar values after a glucose tolerance test ranged between 41 and 51 mg per 100 cc. Allen points out that the hyperinsulinism in any patient who can be treated by a high protein diet must be very mild. As an incidental experiment, he tried to improve the circulation of diabetic patients with deficient arterial blood supply by the administration of Antuwin S, without favorable results.

RESPIRATORY QUOTIENT AND CARBOHYDRATE METABOLISM

In recent unreported studies carried on jointly by the Carnegie Nutrition Laboratory and our clinic, the results obtained after the administra-

FINANCIAL STATEMENT

RECEIPTS

January 1, 1941 — balance forward	\$119.68
Belknap County	204.00
Carroll County	84.00
Cheshire County	180.00
Coos County	222.00
Grafton County	426.00
Hillsborough County	762.00
Merrimack County	450.00
Rockingham County	336.00
Strafford County	186.00
Sullivan County	120.00
Net receipts, 1940 annual meeting	248.42
Cash received at annual meeting	96.00
Receipts from members not in county societies	30.00
Receipts from trustees from General Fund	1000.00
Refund, Cancer Commission	7.43
Refund, 1940 annual meeting	7.00
Women's Auxiliaries	75.00
	<hr/>
	\$4553.53

EXPENDITURES

<i>New England Journal of Medicine</i> (journals)	\$575.60
<i>New England Journal of Medicine</i> (tables)	26.60
<i>New England Journal of Medicine</i> (transactions)	560.34
<i>New England Journal of Medicine</i> (half-tone cuts)	17.48
Carleton R. Metcalf (salary)	400.00
Bridge and Byron (printing)	106.05
Envelopes and stamps	45.46
Frank J. Sulloway (committee lunches)	8.40
Eagle and Phoenix Hotel Co. (committee lunches)	8.75
Robert O. Blood (telegrams and telephone calls)	19.02
Robert O. Blood (clerical work)	150.00
Women's Auxiliary	100.00
Benevolence Fund	359.50
Florence McCann (Committee on Education and Hospitals)	20.69
The Barwood Press (Committee on Education and Hospitals)	4.50
Phaneuf Press (books)	483.14
Concord Photo Engraving Co. (half-tone cuts)	38.52
Deering G. Smith (preparedness expenses)	186.51
Deering G. Smith (dues collected at annual meeting)	42.00
Warren H. Butterfield (dues collected at annual meeting)	28.00
Leslie K. Sycamore (dues collected at annual meeting)	14.00
George C. Wilkins (cancer committee)	50.00
Carpenter Hotel (entertainment of out-of-state guests)	25.40
Manchester Country Club (expenses at buffet lunch)	955.46
Stanley B. Weld (expenses at annual meeting)	10.00
Augustus Thorndike (expenses at annual meeting)	5.00
Elmer J. Brown (expenses at annual meeting)	113.00
Deering G. Smith (expenses at American Medical Association meeting)	99.45
National State Capitol Bank (service charges)	3.00
	<hr/>
	\$4455.87
Balance January 5, 1942	97.66
	<hr/>
	\$4553.53

The Society is in good financial condition, with a balance of \$97.66 on January 5, 1942. The Benevolence Fund on the same date amounted to \$1385.69. Of this amount, the principal is \$991.19, and the accrued income is \$394.50. During the past year, we have received \$75.00 for this fund from the women's auxiliaries of the following counties:

Merrimack	\$35.00
Strafford	10.00
Rockingham	20.00
Coos	10.00

We gave \$100.00 to the State Auxiliary to cover in part the expenses of its meeting last May.

There were two unpaid bills on January 1, 1942, owing to the fact that our expenses were heavier than usual at the one hundred and fiftieth anniversary. These bills, whose total amount was \$400.08, have since been paid.

One officer and one former officer of the Society have died since our most recent meeting: Robert M. Deming, of the Committee on Tuberculosis, died on January 28, 1942, and Frank E. Kittredge, a former president, died on July 8, 1941.

The President chose Ralph W. Tuttle, of Alton, for Anniversary Chairman.

A year ago, the House of Delegates made the following recommendations, which have been carried out:

Dues were remitted for members who during any part of the year were in the Service.

The New England Medical Council was eliminated from the standing committees.

A Committee on Public Health was appointed, which has been co-operating with the State Board of Health.

The Committee on Child Health and the Committee on Maternity and Infancy have been made standing committees instead of special committees.

Fifty dollars was given to the Cancer Committee for its work.

The Committee on Public Relations and the Committee on Medical Economics conferred with Mr. Sulloway and have written an enabling act to cover the cost of medical care.

The Committee on Medical Economics conferred with the Farm Bureau about sickness insurance for farm families, but the Farm Bureau has apparently dropped the plan and has shown no recent interest in putting it into effect.

The Committee on Medical Relief has been disbanded. Its work has been referred to the Committee on Medical Economics.

Since the last annual meeting, the Benevolence Fund has received \$1.00 from every member who has paid his dues.

On July 9, 1941, the Trustees removed \$3000 of the Benevolence Fund from the Savings Bank and invested this amount in United States Savings Bonds. On the same date, \$1000 was removed from the General Fund to pay the expenses for the one hundred and fiftieth anniversary.

Dr. Adolphe J. Provost, of Manchester, was appointed a member of the Medical Advisory Committee on Eye Diseases to co-operate with the State Department of Welfare.

I have referred to the Committee on Communications and Memorials two problems of membership. One of our elderly members has been afflicted with cerebral thrombosis and would like to become an affiliate member. He

is, however, one of five members who joined the Society before a county society had been formed in his territory. The by laws make it compulsory for a county society to recommend a man for affiliate membership before the House of Delegates can vote on such a matter.

The other case concerns a doctor in another state who was originally a resident of New Hampshire. One of the county societies elected him an honorary member, but he desires to pay his dues. Some definite conclusion should be reached on these two cases and on similar cases that may arise in the future.

We have eleven standing committees and two rotating committees. It seems inconsistent to have the Committee on Medical Economics and the Committee on Medical Education and Hospitals rotate each year. Should not these committees be standing committees?

CARLETON R. METCALF, *Secretary Treasurer*

On motion duly made and seconded, it was voted that the Secretary be instructed to read the communication from the Treasury Department, Bureau of Narcotics, before the Society.

Dr. Dye spoke as follows:

An agent of the Bureau of Narcotics visited the State Board of Registration in this connection a couple of days ago. I believe last year the House of Delegates decided against recommending approval of the Uniform Narcotic Act for New Hampshire, because of the amount of red tape engendered in carrying out such an act. However, it is obvious from this letter and from the report unofficially made to us by the representative of the department that the doctor is liable for all the representations that come to him in the way of dispensing narcotics.

At the moment, there is nothing in the state law that will enable the State or a federal prosecutor to hold, in the state's name, an addict who falsely obtains, by the nature of fraud or intention of fraud, a prescription for narcotics from a licensed practitioner in the State. I should like to recommend either further discussion or for a motion, as is seen fit, that the House of Delegates recommend to the State that an amendment be passed to our present narcotic law, that any person who secures a narcotic prescription from a physician, with the intent of actual fraud or intent to fraud, shall be prosecuted by the State.

I believe that would help the situation tremendously. Case after case was reported to us in which a smooth talking person, more or less of a confidence man, would approach some member of our profession in the State and would secure from him a large narcotic prescription. This person, in turn, would go to a drug store and purchase the narcotics. He would be apprehended by a man who represented, as an investigator, the Bureau of Narcotic Control, and found that this prescription was not necessary for him. But, according to our state law, there was nothing that the investigator could do to hold this person, who had secured a prescription by fraud. The only thing in the law would be to take some punitive measure against the physician who issued the prescription.

Therefore, the duty falls on the physician in this state as well as the pharmacist, concerning whether anything shall be done, or any prosecution shall be made for the violation of this law.

Since we have no uniform narcotic act, and since any smooth confidence man may come into the State, get a prescription and have it filled and not be liable, we

are more or less open to having many of these fraudulent addicts come here and put us on the spot, with regard to prosecutions.

Therefore, I believe that some action should be taken by the House of Delegates on this recommendation.

Dr. D. G. Smith seconded Dr. Dye's motion and stated that there are forty-three or forty-four states in which the man who obtains the narcotic or prescription is liable for prosecution. New Hampshire and Vermont are two of the states in which there is no penalty for a man coming in and obtaining a prescription. The result is that such persons are already beginning to flock into New Hampshire and Vermont, buying the morphine and taking it to Boston and peddling it there.

Dr. Sycamore asked if there were a uniform narcotic law that is recommended by the Federal Bureau.

Dr. Dye answered that a uniform narcotic act came up before the House of Delegates last year and was voted against because it entailed a good deal of red tape. It would require a full-time man in the Health Department, with much expense to the State. There would also be a considerable amount of red tape for each physician regarding making out of forms and so forth. The State Board of Health is more or less against a uniform narcotic act; it does not believe that the State is large enough to warrant such a law. It is believed that some amendment to the present law, to make persons who obtain prescriptions by fraud liable to prosecution, would be sufficient.

The President asked if that released the doctors from their responsibility.

Dr. Dye replied that it did not but that, at the moment, the addict is not held to prosecution at all, whereas the doctor has all the responsibility.

Dr. Sanders asked whether everything could be covered so that the addict could not escape the responsibility and how fraud on his part could be proved.

Dr. Metcalf answered that the amount obtained was proof. For example, when a man buys 100 tablets of morphine, $\frac{1}{2}$ grain each, he is considered an addict.

The motion was carried.

The Committee on Officers' Reports commended the faithful and efficient work of the Secretary-Treasurer and recommended that, at the next revision of the by laws, the Committee on Medical Economics be changed from a rotating to a standing committee.

Dr. D. G. Smith suggested that the Committee on Medical Education should also be changed.

Dr. Dye moved that both committees—the Committee on Medical Education and Hospitals and the Committee on Medical Economics—be made standing committees.

Dr. Sycamore recommended that at the next revision of the by-laws, the Committee on Medical Education and Hospitals and the Committee on Medical Economics be changed from rotating committees to regular standing committees.

Dr. Dye suggested that this matter be referred to the Committee on Constitution and By-Laws, with the request that it be reported the following day.

Dr. Sycamore accepted the amendment.

This motion was duly seconded and was carried.

Because of the amount of business to be transacted, it was voted to omit the reading of the councilors' reports.

Reports of Councilors

BELKNAP COUNTY

The Belknap County Medical Society held six meetings from November to April inclusive. The meetings were all well attended, and the excellent quality of papers was maintained. A different member was responsible for each meeting.

The Society lost one member by death and gained four new members.

C. S. ABBOTT

CARROLL COUNTY

The Carroll County Medical Society held its meetings as usual.

Our membership is small but our spirit is excellent.

One member is now in the Army Medical Corps, and of course, others may follow.

Our spring meeting has been postponed to a later date than usual because of the absence of our President, but this meeting will be held early in the summer.

CHARLES E. SMITH

CHESHIRE COUNTY

The Cheshire County Medical Society held two meetings during the past year. At each meeting, papers were read by visiting men. Each paper was discussed at length and this added much interest to the meetings.

We have had no increase in membership in the past year. One member is in service at the present time, and several more are awaiting call.

JOHN J. BROSNAHAN

COOS COUNTY

The Coos County Medical Society has not met this year. We are expecting a grand meeting this spring after the State Society meeting. On this account, I have little to report. I am hoping for more interest among the profession this coming year.

RICHARD E. WILDER

GRAFTON COUNTY

The annual business meeting of the Grafton County Medical Society was held at the Grafton County Hospital, North Haverhill, on October 9, 1941. Election of officers took place, and nine new members were received.

A group discussion was led by W. F. Putnam, of Lyme, on "Pitfalls of Medical Practice."

Three other meetings were held during the year. On December 11, the Society met at Hale's Tavern, Wells

River, Vermont, for dinner, and a group discussion on "Common Respiratory Infections" was led by E. C. Campbell, of Woodsville.

The meeting of January 29, 1942, was held at the Littleton Hospital. A discussion on "Uterine Hemorrhage" was led by H. C. Pickwick of Lisbon.

On February 26, the society convened again at Hale's Tavern, Wells River, Vermont. The discussion on "Uterine Hemorrhage" was continued.

The programs of these meetings dealing with everyday problems of general practice were arranged purposely to stimulate discussion and active participation of a larger number of members.

A. W. BURNHAM

HILLSBOROUGH COUNTY

The Hillsborough County Medical Society during the last year has had the largest membership since it was founded. We have at present 146 members.

At our meeting in Manchester, November 18, 1941, we had two very interesting papers, one by Dr. Alfred L. Frechette, on "Venereal Disease Problems in New Hampshire," and one by Dr. Thomas J. Anglem, on "Chemotherapy in Surgery." During the morning session, Dr. Charles H. Parsons gave a very detailed talk on "Medical Organization for Civilian Defense" in this state. This was of great value, and I understand that practically every town in Hillsborough County has a medical setup as part of its civilian defense.

A spring meeting was held at the Nashua Country Club, where Dr. Dolloff, president of the New Hampshire Medical Society, spoke, and where papers were presented by Dr. Charles H. Rammelkamp and Dr. Otto J. Hermann, of Boston.

A very largely attended meeting was held at Alma's Tea Room, Manchester, on April 28. Dr. Deering Smith gave a complete outline of the Procurement and Assignment Service. Interest ran high, as shown by the fact that three hours were taken up in the presentation and discussion of this subject. Dr. W. D. Thibodeau, president of the Hillsborough County Medical Society, complimented Dr. Smith on his excellent presentation.

I am of the opinion from my observation that more interest is being taken in the county meetings. This is shown by an increase in membership and the attendance, which is about fifty at each meeting.

CLARENCE O. COBURN

MERRIMACK COUNTY

The Merrimack County and Center District Medical Society has held four meetings during the past year.

At a meeting on July 2, 1941, held at the Franklin Country Club, Dr. Lewellys F. Barker, professor emeritus of medicine at Johns Hopkins University School of Medicine, spoke on "Heredity." Dr. R. J. Weissman, of Franklin, was voted into membership.

On October 8, a meeting at the Eagle Hotel, Concord, was addressed by Dr. Champ Lyons, of the Massachusetts General Hospital, who spoke on "Chemotherapy." He recommended sulfadiazine as the drug of choice. Dr. W. H. Norton, of Andover, was admitted to membership. It was voted to send \$100.00 to the National Committee for Extension of Medical Service.

On January 7, 1942, the annual meeting was held at the Eagle Hotel. Dr. Edward Putnam was elected president, Dr. Philip Forsberg was elected vice-president, and Dr. Warren Butterfield was re-elected secretary-treasurer. Dr. Charles H. Dolloff, president of the New Hampshire Medical Society, spoke briefly. With Dr. Carroll Cilley,

county commissioner, as guest, the present day relief problems were discussed at considerable length. Drs Bland, Morrity and Philbrook, of the State Hospital Staff, were elected members of the Society.

On April 1, 1942, a meeting was held at the Eagle Hotel. At the request of the Auxiliary, future meetings are to be held on the first Tuesday of the month. Dr Deering Smith, of the Procurement and Assignment Service, spoke on medical enlistments. In recognition of his long membership and service to the profession, Dr Chancey Adams was presented with a suitable gift.

HENRY H. AINSDEN

ROCKINGHAM COUNTY

The annual meeting of the Rockingham County Medical Society was held at the Mitchell Memorial Hospital, Brentwood, on December 17, 1941. Officers for the following year were elected, and four new members were admitted. Luncheon was served by the county commissioners and superintendent.

The afternoon session was devoted to a discussion of the medical defense setup in this county. In outlining plans for the organization of medical defense units, consideration was given to the necessity of some unification of system and the recommendation was made that each community take suitable steps regarding equipment trained workers and physicians at hand.

The spring meeting of the society was held at Exeter Hospital on April 28, 1942. Twenty eight members were present. At the business meeting, following a discussion concerning the methods used and the extent to which chiropractors were encroaching on the practice of medicine in Rockingham County, a motion was adopted instructing the county's delegation to bring this matter to the floor of the State Society House of Delegates for action.

After further discussion, a motion was adopted instructing the County Delegates to bring to the attention of the State Society House of Delegates the problem of medical officers in the United States Navy practicing private medicine while on duty. There was evidence that such practice was occurring at Portsmouth Navy Yard. It was further requested that a ruling on this matter be obtained from the Navy and War departments from the Commandant, Portsmouth Navy Yard, and from the State Board of Registration in Medicine. One new member was admitted.

After luncheon at the hospital, Dr D. G. Smith of Nashua, Chairman of the New Hampshire Procurement and Assignment Service, gave a detailed resume of the present status demands of the Government on New Hampshire physicians for war service. He stated that the quota for the next sixty days was fifty doctors, and warned that more would be called for, urging full co-operation to help fill the immediate quota of the State under the direction of the medical profession itself, rather than under assumption of powers of draft by the government authorities.

CLEON W. COLE

STRAFFORD COUNTY

The Strafford County Medical Society had for the year 1942 thirty four active and six affiliate members.

The annual meeting was held on October 22, 1941, at the University Commons, Durham, New Hampshire. It was the one hundred and twenty fourth annual meeting of the society and was attended by twenty three members and a guest. Dr Charles H. Dolloff, president of the

New Hampshire Medical Society, presented informative material regarding the Newer Treatments of Mental Disorders.

A special meeting of the society was held on March 8, 1942, at the American House, Dover, New Hampshire. Twenty one members were present. The purpose of this meeting was to discuss and act on an increased fee table for medical services in Strafford County, the fees then existing being lower than the usual fees elsewhere in New Hampshire. A new minimum fee schedule was adopted and went into effect on March 15, 1942.

The spring meeting was held at the new Frisbee Memorial Hospital in Rochester, New Hampshire, on April 29, thirty one members and guests being present. After the usual business meeting, Dr Samuel Levine presented an excellent paper on Heart Disease Electrocardiography and the General Practitioner, a lecture of great service to those present. Dinner was served by the hospital authorities and the local doctors conducted the out-towners on a tour of the hospital. Rochester may well be proud of this beautiful gift to their community.

There were no deaths among our members during the fiscal year.

Dues were all paid promptly and disbursed to the state society treasurer on February 3, 1942.

J. A. HUNTER

SULLIVAN COUNTY

The Sullivan County Medical Society enjoyed its usual activity during the past year. All physicians practicing in the county are members of the society, and the percentage of attendance at meetings is always high.

At the annual meeting held in Claremont, we were honored in having as our guest Dr. Charles H. Dolloff, of Concord, president of the New Hampshire Medical Society, who spoke on Medical Defense and other timely subjects.

In addition to the election of officers for the coming year there was a scientific program with free discussion by many of the members.

Luncheon was served at the Claremont General Hospital. Our next meeting will be held at Charlestown during the summer.

EMERY M. FITCH

In the absence of Dr. Woodman, Dr. Dye stated that the members of the Committee on Amendments to the Constitution and By Laws knew of no necessary amendments to the constitution and by laws that should be brought up for this year.

In the absence of Dr. Stewart, Dr. Sycamore read the report of the Committee on Child Health.

Report of the Committee on Child Health

The Committee on Child Health co-operated in the presentation of a series of radio talks on various aspects of child health, given under the auspices of the New Hampshire Congress of Parents and Teachers and the New Hampshire Pediatric Society. These were broadcast over Station WFEA, beginning in October and continuing into February.

At a meeting on February 18, the recommendations of the Children's Bureau regarding immunization of children as a war measure were considered as they applied to New Hampshire. It was agreed

1. That it would be desirable to have all children over nine months of age immunized against diphtheria and smallpox;
2. That it would be better to defer any large-scale attempt at immunizing against tetanus until a uniform system of tagging such children could be worked out for the country as a whole;
3. And that immunization against typhoid fever could be deferred until such time as evacuation of cities became necessary, and could then best be done at evacuation centers as a mass procedure.

COLIN C. STEWART, *Chairman*
 TRAVIS P. BURROUGHS
 FRANKLIN N. ROGERS

Dr. Sycamore stated that the Committee on Officers' Reports commended as a valuable educational method the activities of the Committee on Child Health in co-operating in the presentation of radio broadcasts.

The conclusions of the committee regarding immunization of children as a war measure were approved, and it was recommended that the House of Delegates instruct the Committee on Child Health and the Committee on Public Health to confer with and co-operate with the appropriate State and Federal agencies, with a view to carrying out the immunization against diphtheria and smallpox of all children over nine months of age.

Dr. Sycamore moved the adoption of this portion of the report.

This motion was duly seconded and was carried.

Report of the Committee on Public Health

The Committee on Public Health is a new one, being first elected in 1941; no one on the committee knew its duties or its function. Communication with Dr. Metcalf, secretary of the New Hampshire Medical Society, concerning its duties referred us to Dr. Burroughs, of the State Board of Health, and after some thought we are of the opinion that we are liaison officers between the New Hampshire Medical Society and the State Board of Health.

We have had five meetings in Concord. The first was held at the office of Dr. Burroughs at the State House on September 26, 1941. Drs. Burroughs, Frechette, Vintner, Powers and Smart were present. The discussion was concerned mainly with whether or not the New Hampshire Medical Society, as represented by the Committee on Public Health, would recommend or sanction the Board of Health, with the aid of the New Hampshire Tuberculosis Association, to make mass x-ray studies in any or all industries requesting such examination in an attempt to find patients affected with tuberculosis. The Venereal Division is also to be allowed to do the routine blood Wassermann examinations. Patients, after the above check, are to be referred back to their own physicians. After much discussion, it was decided to inquire of other states their experience regarding the cost of such studies and the reactions of the physicians in the states that have held these industrial examinations.

This meeting was then adjourned.

The second meeting was held on September 30, 1941, in the same location and Drs. Burroughs, Vintner, Powers and Smart were present. The above-mentioned program

was discussed and Dr. Metcalf, secretary, was called in to give his advice, which was that the present policy of the New Hampshire Medical Society would, he thought, be against the State Board of Health's taking over such a program. New Hampshire is one of the most highly developed industrial states, having about 142,000 on the employees' compensation roll. It seems to your committee that such an ambitious program of mass x-ray films would entail a large expense, and we are of the opinion that in this time of war upheaval it might be better to await a more thorough investigation by the Committee on Public Health concerning the time and desirability of such a program.

The second important question that came to your committee's attention was that of having the State Board of Health, in collaboration with the Committee on Public Health, formulate certain minimum requirements for first-aid rooms in industries so that there would be some place in the State where such guidance could be found for industries that are now trying to establish their first-aid accommodations. An outline has been drawn up, and your committee recommends that the Medical Society adopt this plan.

Another meeting was held on March 13, 1942, in the Governor's Council Chamber at call of John J. Hallihan, of the Department of Public Welfare, a committee appointed by the Governor to accumulate firsthand knowledge of the tuberculosis situation in New Hampshire, and especially the sanatoriums; two weeks later, your committee inspected the Pembroke Sanatorium, and later was requested to inspect the Glenduff Sanatorium. This study is incomplete, and no report is possible at present.

Finally, the National Council on Industrial Health requests that the Society send a representative to its fifth annual meeting, and it is the opinion of your committee that, if the New Hampshire Medical Society desires an active and progressive public-health committee, it authorize the sending of such a representative to this meeting.

CHESTER L. SMART, *Chairman*
 HARRIS E. POWERS

Dr. Sycamore stated that the Committee on Officers' Reports commended the members of the Committee on Public Health for the vigorous and judicious activities of this new committee. Their decision that further study should be given to the question of mass x-ray and serologic examinations in industrial establishments was approved.

Dr. Sycamore recommended that the House of Delegates approve the collaboration of the Committee on Public Health with the State Board of Health in formulating minimum requirements for first-aid rooms in industries.

In view of the importance of industrial health in the war effort, it was recommended that the committee be authorized to send a representative to the National Council on Industrial Health, the expenses of the representative to be defrayed by the Treasurer.

A motion to adopt this portion of the report was duly seconded and was carried.

Dr. Benjamin P. Burpee then presented the report of the Committee on Maternity and Infancy.

Report of the Committee on Maternity and Infancy

There was a gratifying reduction in the maternal death rate for 1941. For eight years, the committee has studied and analyzed every maternal death reported, making an effort to appraise, so far as possible, the problems relating to causes of death among mothers and infants.

Each year, the committee has made its report to the New Hampshire Medical Society, but in the past five years, including 1942, the report has been printed and distributed widely to physicians, hospital superintendents, and nurses. It is our opinion that the results shown and recommendations made—based on findings in the analysis of each case—have been of definite assistance to many physicians in the conduct of obstetric practice. For the past two years, the committee, through its agent, has corresponded with each physician reporting a maternal death with the view to making such suggestions or rendering such consultation as may be of value. Many physicians have responded with interest and gratitude for the suggestions and recommendations of the committee. During the past year, there was an unusual display of co-operation, every physician and hospital being most willing to supply the committee with all possible help and information.

As in the past, the study was conducted by the committee through an agent, the only person knowing the identity of the physician and patient or hospital. That person is the Director of the Division of Maternal and Child Health of the State Board of Health. Each case was studied objectively and thoroughly, the committee endeavoring to analyze the facts and draw conclusions from those facts. In some cases, obviously, no definite conclusions regarding the exact cause of death could be made. This was true chiefly in cases in which no autopsy findings were available. However, the committee endeavored to classify each death.

Prevention of maternal and infant deaths is, of course, the prime concern of all. In this analysis, it is encouraging to note that most of the deaths were in the classification of unavoidable and that many were due to accidents of pregnancy.

The study of infant deaths and stillbirths was less thorough because it was impossible to gather complete data on such large numbers of cases. The best that could be done was to appraise the deaths by means of the causes reported. In the report, the deaths are tabulated as to causes, and some conclusions were drawn from such a tabulation.

Stillbirths were analyzed from the data secured from questionnaires sent to physicians reporting stillbirths. Most questionnaires were filled out and returned, but some information is lacking from others. A tabulation of stillbirths as to reported causes follows in the report.

It should be understood at the beginning that the remarks and recommendations of the committee are entirely impersonal and objective, since the committee did not know the identifying information for any case reported.

The record of marked decreases in maternal mortality is of special significance in view of the present emergency and under war conditions. With the possible disruption of family life, changes of large groups of population, housing and sanitary problems resulting from possible crowding in defense areas in the State, the inevitable shortage of medical and nursing personnel in many areas may show serious effects on family life in New Hampshire, as elsewhere, and may cause a rise in maternal and infant mortality. The new low rate of 1.8 per 1000 live births for New Hampshire may therefore serve not only as a measure of past accomplishments but also as a means of pointing to the possibilities in meeting the difficult problems of the future.

This low rate is significant not only in terms of fewer maternal deaths but also in that the birth rate in the State was higher than at any time since 1920. It is the hope of the committee that despite problems and difficulties arising out of the war, physicians and hospitals will not relax their standards of good care, but will in fact press every effort to advance toward better obstetric practice.

During the year, the committee held five meetings.

MATERNAL DEATHS

In 1941, there were 17 maternal deaths. During that year, there were 9616 live births. The rate for maternal mortality was therefore 1.8 per 1000 live births. Each of the 17 deaths was studied and classified according to the *International Classification of Causes of Death* (fifth revision). These deaths were reported for the calendar year ending December 31, 1941. Following an appraisal and scrutiny of each case, the committee reclassified the deaths into categories of causes according to the data received and conclusions drawn from the data, as follows:

Code No.	Cause of Death	No. of Deaths
140 (c)	Abortion (self induced)	2
140 (d)	Abortion (not self induced)	1
144 (a)	Toxemia of pregnancy with convulsions—death before delivery	2
148 (a)	Toxemia of pregnancy—death after delivery	1
146 (c)	Placenta previa (post partum hemorrhage)	2
146 (e)	Post partum hemorrhage	2
147 (b)	Puerperal sepsis	1
144 (d)	Puerperal embolism	2
149 (a)	Accidents of pregnancy (inversion of uterus)	1
149 (f)	Accidents of pregnancy (malposition cesarean section embolism and so forth)	3
		<hr/> 17

In order of frequency of cause as determined by the careful analysis of each case, the committee reclassified them as follows:

Cause of Death	No. of Deaths
Toxemia of pregnancy (all types)	4
Accidents of pregnancy	5
Puerperal embolism	2
Inversion of uterus	1
Transverse position	1
Post partum hemorrhages	3
Placenta previa	1
Retro placenta	1
Cause undetermined	1
Abortions	3
Cesarean sections	1
Puerperal sepsis	1
	<hr/> 17

Only two cesarean sections were performed in the 1941 series of maternal deaths. One was performed for a good indication, but one was done for what the committee considered no proper indication.

In the series, only three autopsies were performed.

As in the past all cases were further classified into three categories—Group I, those in which the patient was at fault because of refusal of prenatal care, neglect, or self-induced abortion and so forth; Group II, those in which the obstetric treatment was inadequate; Group III, those which were apparently unavoidable,—as follows:

Classification	No. of Deaths
Group I	4
Group II	5
Group III	8
	<hr/> 17

The causes of death in Group I, in which the patient was at fault, were as follows:

Cause of Death	No. of Cases
Induced abortion	3
Toxemia of pregnancy (treatment refused)	1
	<hr/> 4

The causes of death in Group II, in which the obstetric care was inadequate, were as follows:

CAUSE OF DEATH	NO OF CASES
Post-partum hemorrhage	1
Cesarean section	1
Puerperal septicemia	1
Toxemia	2
	5

The causes of death in Group III, in which the deaths were apparently unavoidable, were as follows:

CAUSE OF DEATH	NO OF CASES
Inversion of uterus	1
Acute pulmonary edema	1
Pulmonary embolism	1
Puerperal sepsis	1
Post-partum hemorrhage	2
Chronic nephritis	1
Cesarean section (obesity)	1
	8

Some gratifying facts are noted concerning the causes of deaths as classified in the foregoing tables. In the first place, the majority of deaths were undoubtedly accidents of pregnancy. Coming under this group are of course the embolic phenomena, malpositions, inversion of the uterus and adherent placentas. There was less evidence that really poor obstetrics was practiced in the handling of such problems in this series of cases, as compared with past series. The medical profession would like to believe that the increasingly lowered death rate is due to better obstetrics.

Toxemias continued to be proportionately the chief cause of death in New Hampshire. The largest number of deaths were due to accidents of pregnancy. In the United States as a whole, infections were the chief cause of death, causing 41 per cent* of the maternal deaths in 1940 (figures for 1941 for the United States as a whole are not available). As compared to infections, the toxemias caused 25 per cent of maternal deaths in the country as a whole in 1940, and post-partum hemorrhage was the cause of 23 per cent.

Because toxemias still present the greatest problem, the committee believes that recommendations regarding accepted methods of treatment should be reiterated in this report; this follows below.

If accidents occurring in pregnancy, at the time of delivery or in the post-partum period are excluded, the other deaths recorded were for the most part preventable. Induced abortions are surely unnecessary, and should be vehemently stopped. It does present a real problem in the efforts of the profession to reduce maternal mortality. The medical profession should not rest until every preventable cause of maternal death is reduced to an absolute minimum.

In the 1941 series, 15 patients were delivered in hospitals, and 2 in the home. The following data on urban and rural residency are also of interest:

COUNTY	URBAN CASES	RURAL CASES	TOTAL CASES
Belknap	0	0	0
Carroll	0	1	1
Cheshire	4	2	6
Coos	1	1	2
Grafton	2	0	2
Hillsborough	4	0	4
Merrimack	0	0	0
Rockingham	1	0	1
Strafford	1	0	1
Sullivan	0	0	0
	13	4	17

To illustrate the trend in maternal mortality statistics, the following data are presented:

YEAR	NO. OF DEATHS	MATERNAL MORTALITY RATE PER 1000 LIVE BIRTHS
1930		6.2
1932		5.4
1933		6.3
1934		5.4
1935		6.1
1936	46	4.8
1937	37	4.8
1938	34	4.3
1939	24	3.8
1940	25	3.1
1941	24	2.8
	17	1.8

Data are available from the United States Bureau of the Census for maternal deaths for 1940. It is of interest that, in a comparison of percentage decrease in maternal deaths for the period of 1931-35 with 1936-40, New Hampshire had a 37.5 per cent decrease in the latter period. The maternal death rate in 1931-35 was 6.27 per 1000 live births, as compared with 3.92 in 1936-40. With the present low maternal death rate of 1.8 per 1000 live births, this percentage decrease is most gratifying. New Hampshire is grouped with the states that show a percentage decrease of 35 per cent or more for the period.

These census figures further indicate that for 1940, 11 per cent of the total maternal deaths were due to abortions and 7 per cent were due to ectopic gestation; 26 per cent of patients died before delivery, and 56 per cent died during or after delivery. It seems that many of the 56 per cent of deaths occurring during or after delivery could have been prevented. Many of the deaths in this period were due to infection.

In next year's report, it may be possible to include figures based on these problems for the 1941 deaths. Such figures have not as yet been analyzed.

The increasing and apparent downward trend in maternal mortality rates is significant statistically, and it can be inferred that better obstetric care, more adequate hospital facilities, better quality of nursing care and improved methods of treatment are most presumably responsible. These efforts must continue with all the vigor of the profession and agencies engaged in educational health work for the civilian population.

One outstanding improvement should be commented on. This is a matter of hospital records. It was definitely apparent that better records, more complete information, more laboratory findings and so forth were available in hospital cases. Physicians are still found to keep very inadequate or no records. Physicians should realize that good records are not only indispensable in the intelligent care of a patient but also a protection to the physician in the event of legal procedures.

As reported for last year, hospital facilities have improved markedly. Several hospitals have built new wings for maternity and infant care; better fire protection was provided, and New Hampshire has a new well-equipped hospital to add to its facilities. On the whole, the care of maternity patients has shown an encouraging improvement. The efforts of public-health agencies regarding such improvement are well worth mentioning.

In most cases, more prenatal care was sought by patients and provided for by the medical profession.

RECOMMENDATIONS AND COMMENTS

Recommendations of the committee and comments on problems arising have been considered of value to physicians reporting their numerous problems and to those who are aware of difficulties connected with the puerperium. This year, the recommendations are based on

*Figures obtained from United States Bureau of the Census.

actual case studies analyzed from data collected and presented herein by way of illustration. The comments arose from the objective conclusions arising out of the study. The more important recommendations of past years are also included for emphasis by repetition.

The committee recommends that no attempt be made at the delivery of a central placenta previa from below in either a primipara or a multipara.

It is recommended that in cases in which an adherent placenta occurs, 1 cc pituitary extract be given at two hour intervals and accompanied by the Crede maneuver only at the same time that pituitary extract is given. This should be tried before any attempt at manual removal is made. Manual removal is unjustifiable under 12 hours unless there is excessive and uncontrollable bleeding. The Crede maneuver, moreover, should be performed with care and skill, so as to avoid trauma of the uterus.

The committee disapproves of the use of vaginal or cervical packs. The danger of masking the bleeding into the uterus and of subsequent infection is feared by such methods.

Cesarean sections should not be performed without competent consultation and without absolute indication. The committee believes especially that a section should not be done when the membranes have been ruptured for twenty-four hours.

Versions should not be done unless the patient is deeply anesthetized.

The committee believes that most occiput posterior positions will right themselves or deliver spontaneously if enough time is allowed and watchful waiting considered.

The committee recommends that autopsies be performed on every maternal death.

In addition to recommendations based on the 1941 study, the committee reiterates that physicians should keep better and more useful records, that hospitals require consultations for operative deliveries, and that when hospital facilities are available, every possible effort be made in the diagnosis and intelligent treatment of toxemias, anenias malpositions, infections and other complications of pregnancy.

INFANT MORTALITY

The following is a tabulation of causes of deaths in infants as reported on the death certificates. These are divided into periods as to when the deaths occurred in relation to birth for those under one year of age.

CAUSE OF DEATH	NO. OF DEATHS
Deaths occurring on or before the first day of life	
Prematurity	98
Congenital deformity	71
Asphyxia	8
Other	7
Cerebral hemorrhage	6
Unknown	3
Birth injury	2
Hemorrhage of newborn	1
	<hr/> 151
Deaths occurring in the first month exclusive of the first day	
Prematurity	16
Congenital deformity	16
Cerebral hemorrhage	9
Asphyxia	3
Atelectasis	4
Intestinal obstruction	2
Gastroenteritis	2
Pneumonia	8
Other	2
Malnutrition	2
Syphilis	1
	<hr/> 70

Deaths occurring from the second to the twelfth month inclusive	
Pneumonia	36
Other	12
Gastroenteritis	13
Malnutrition	10
Suffocation	9
Congenital malformations	8
Whooping cough	5
Unknown	4
Septicemia	1
	<hr/> 98

The total number of infants who died in 1941 under one year of age is 319, in 1940, there were 274 deaths. This is a challenging increase. The largest single cause of death is still given as prematurity, and it is interesting that as many as 9 infants died of suffocation from carelessness. Many of the congenital deformities were due to congenital heart disease.

The infant death rate for 1941 is 33 per 1000 live births.

The infant mortality rates per 1000 live births by years are as follows:

YEAR	RATE
1935	54
1936	47
1937	48
1938	48
1939	45
1940	32
1941	33

STILLBIRTHS

Two hundred and eighty one stillbirths were reported in 1941. Questionnaires were sent to all physicians reporting stillbirths, and answers were received for 182 cases.

The causes of stillbirths were tabulated as follows.

CAUSE	NO. OF CASES
Prematurity	24
Congenital deformity	34
Instrumental delivery	13
Toxemia	13
Cerebral hemorrhage	6
Deformities of placenta or cord	50
Unknown	20
Other	16
	<hr/> 187

The number of stillborn infants reported from year to year varies markedly. Many of the stillbirths this year were reported on the questionnaires as due to abnormalities of the placenta or accidents caused by a twisting of the cord about the baby's neck. The committee does not believe that such conditions constitute real causes for stillbirths. A large number of infants died without any apparent or proved cause, even after autopsy findings were recorded.

Stillbirths for the past few years were as follows:

YEAR	NO. OF CASES
1937	181
1938	242
1939	211
1940	187
1941	281

No conclusions can be drawn concerning this variation.

The committee wishes to express its gratitude and satisfaction for the excellent record shown in New Hampshire in 1941 concerning reduced maternal mortality. Appreciation is expressed for the co-operation of physicians and hospitals in making this report possible, and for the encouraging improvements in hospital facilities and better obstetric practices. As in the past, thanks should be given for the co-operation of the Division of Maternal and Child Health of the State Board of Health, whose facilities and personnel were used by the committee in making this study and in preparing this report.

ROBERT O. BLOOD, Chairman
BENJAMIN P. BURPEE
MARION FAIRFIELD

(To be concluded)

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28311

PRESENTATION OF CASE

First admission. A fifty-eight-year-old Polish housewife was admitted to the hospital because of weakness and shortness of breath of three years' duration.

Seven years before entry, the patient fractured her right humerus while pushing away a heavy object. In the next few years, she began to have various body aches, centering in the lower part of the back, shoulders, arms and legs. These aches were not related to posture, fatigue or exertion. There was insidious onset of slight weakness and shortness of breath on exertion. Two years before entry, the patient slipped while scrubbing a floor, and sustained another fracture through the upper right humerus. At that time, roentgenograms taken by a physician showed extensive bone destruction of the proximal half of the humerus by a trabeculated cystic lesion, and similar destructive processes in the right seventh rib, the proximal end of the left femur, and the right and the left ilium. There was also an old fracture of the right clavicle. The patient was given roentgen-ray therapy in nine doses over a period of two weeks in total amounts of 1600 r to the left femur, 1800 r to the right humerus, and 3500 r to the right and left parathyroid regions (half to each side); there was tanning of the skin. Roentgenograms taken nineteen months before entry showed new-bone formation in the areas of destruction noted earlier in the right shoulder, but no change in the lesions in the pelvis. Thirteen months before entry, an additional treatment of 1200 r was given to the parathyroid regions. Fourteen months before entry, blood examinations by another physician showed a red-cell count of 2,600,000 with 55 per cent hemoglobin, and a white-cell count of 3300. The serum calcium was 11 mg. and the phosphorus 3.5 mg. per 100 cc., and the phosphatase was 1.5 Bodansky units. The patient was given large doses of dicalcium phosphate and vitamin D, with progressive relief from body aches. Courses of liver-extract injections, daily doses of ferrous sulfate and three blood transfusions were also given, but there was only transitory improvement in the blood picture. In the two years preceding entry, the patient had several attacks of

severe sharp pain in the lumbar region, not relieved by mustard plasters. She had no chills, fever or hematuria in association with these attacks; however, about a year before entry, there was blood in the urine on several occasions when there was no back pain. She never passed gravel. There was no polydipsia.

The past and family histories were irrelevant. The menses were normal until the menopause ten years before entry.

On admission, the patient appeared elderly and obese. The mouth was edentulous, with pale mucous membranes. There were palpable thickenings of the midportion of the right clavicle and upper right humerus. A single small node was palpable in the right axilla. The heart and lungs seemed normal. The tip of the spleen was easily felt beneath the costal margin in the anterior axillary line. It was firm and not tender. The abdomen and extremities were otherwise normal. Pelvic examination showed a large laceration of the cervix, with surrounding erosion.

The blood pressure was 150 systolic, 90 diastolic. The temperature was 100°F., the pulse 92, and the respirations 20.

Examination of the blood showed a red-cell count of 2,130,000 with 7.4 gm. hemoglobin and 2.8 per cent reticulocytes. The red cells showed stippling and polychromasia. The white-cell count was 2200 with 69 per cent polymorphonuclears, 26 per cent lymphocytes and 3 per cent monocytes. The blood Hinton reaction was negative. The formol-gel test was negative. The blood calcium was 14 mg. and the phosphorus 1.5 mg. per 100 cc., the phosphatase 5.4 Bodansky units, the serum albumin 4.7 gm., the globulin 2.1 mg., and the non-protein nitrogen 26 mg. per 100 cc. The cholesterol was 159 mg. per 100 cc. The carbon dioxide combining power was 23.1 milliequiv. and the chlorides 107.2 milliequiv. per liter. The van den Bergh reaction was normal. The urine showed a ++++ Sulkowitch reaction (calcium phosphate in urine), but contained no albumin. There were occasional red and white cells in the sediment. The phenol-sulfonephthalein excretion was 50 per cent in two hours. The urine was positive for 10 mouse units of follicle-stimulating hormone per 100 cc. The excretion of 17-ketosteroids was 3.3 mg. per 24 hours. An electrocardiogram was normal.

Roentgenograms of the skeleton showed extensive decalcification, with thickening of the cortex. There was some new-bone formation in the medial portion of the right ilium, and multiple cysts were present in the upper end of the left femur and in both ilia (Fig. 1). The ribs and humeri also contained cysts. The structure of the skull was markedly altered, with indistinctness of the diploë

and blood vessels. There were platybasia and wedge appearance of the dorsal vertebrae. In roentgenograms of the chest, the heart appeared normal. The lung fields showed only apical scars. A rounded mass, 7 cm. in anteroposterior diameter and 6.5

shoulders, with weakness and a sense of heaviness in the chest. Four weeks before readmission, a persistent cold was contracted. Pains then reappeared in the right arm at the site of the old injury, and there was some cramping in the legs.

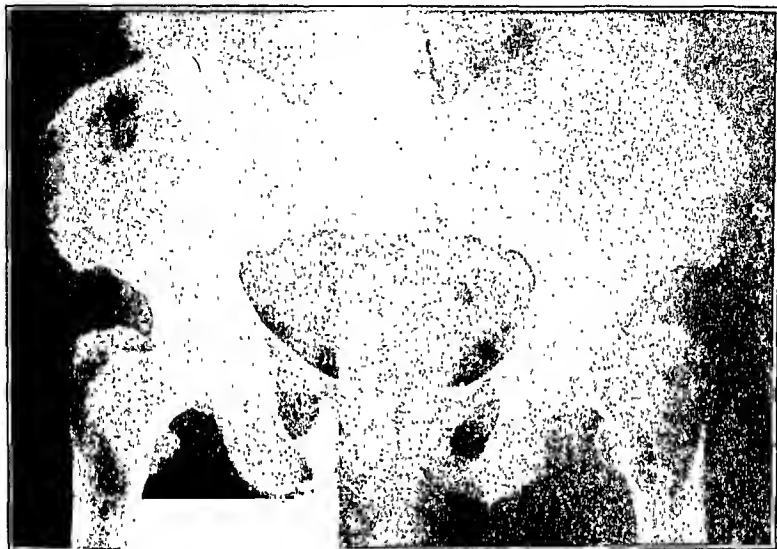


FIGURE 1.

cm. in lateral diameter, lay in the mediastinum below the arch of the aorta and just beneath the sternum. The esophagus showed a traction diverticulum in its middle third. A flat film of the abdomen showed kidney shadows slightly smaller than usual. Two small areas of calcification lay in the region of the lower pole of the left kidney. A laminated gallstone-like structure lay in the liver region. The spleen appeared enlarged. An intravenous pyelogram showed prompt excretion of dye. The pelves and calyces were relatively small, with the aforementioned stone on the left, but were otherwise negative.

The patient was given 1200 r to the anterior mediastinal field, and a similar amount to the posterior mediastinal field. Repeated chemical studies of the blood showed no essential change after the irradiation. The patient was given a blood transfusion and discharged to the Out Patient Clinic.

Second admission (three months later). The patient continued fairly well, and was able to do housework. There was some pain in the back and

There were several slight nosebleeds. The appetite was only fair.

On readmission, physical examination was essentially as before. An area of dullness over the sternum at about the second interspace extended to the left about 2 cm. Laboratory data were essentially as before. Throat, blood and urine cultures were negative. The corrected blood sedimentation rate was 0.9 mm. per minute.

A roentgenogram of the chest showed no essential change in the mass in the mediastinum.

On the twentieth hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. JOSEPH C. AUB: We have here the story of a Polish woman, past the menopause, with progressive fatigue, marked bone and muscle pains, anemia, a large spleen and too few white cells. These findings had lasted for years. She had known that she had bone lesions for two years, and large doses of x-ray therapy did nothing in them. The duration and course of the difficulty

practically rule out the diagnosis of myeloma.

The low 17-ketosteroid excretion puzzles me. It should be higher after the menopause.

DR. FULLER ALBRIGHT: That is all right for a debilitated person.

DR. AUB: Yes, but a little low.

DR. ALBRIGHT: Low for a normal person.

DR. AUB: These x-ray films are fascinating. I should like to ask Dr. Schatzki about the skull and about the feet. What does "platybasia" mean?

DR. RICHARD SCHATZKI: In platybasia, the cervical spine is pushed into the floor of the posterior fossa, like a piston. This occurs during early development.

DR. AUB: Should it help me in the diagnosis?

DR. SCHATZKI: I do not believe so. Whether it may develop later in life, I do not know.

DR. ALBRIGHT: Yes; it does. Any decalcifying process will do it.

DR. AUB: Is that moth-eaten appearance more than normal, according to your technic?

DR. SCHATZKI: Yes.

DR. AUB: What about the toes?

DR. SCHATZKI: I am wondering about them myself. I should say that although the cortex of the skull is definitely thickened, the cortex of the toes is by no means thickened, but thin, and they are decalcified. I should say that the feet show merely marked decalcification.

DR. AUB: Are these trabeculae abnormal?

DR. SCHATZKI: There may be tiny cysts in one of the toes, but actually all you see in the feet can be explained by decalcification.

DR. AUB: Is this traction of the esophagus just where the tumor in the chest is?

DR. SCHATZKI: No; I should say that was a traction diverticulum of the esophagus—it is of no clinical importance.

DR. AUB: They do not fit together—the mass and the traction diverticulum in the esophagus?

DR. SCHATZKI: The mass is in the anterior mediastinum in front of the arch. It has nothing to do with the esophagus. It is far away from the esophagus.

DR. AUB: I think this is a very puzzling case. Of course, the obvious diagnosis is parathyroid tumor. The patient had a high calcium, low phosphorus and a normal phosphatase level in the blood. She had kidney stones, and was passing bloody urine. All these things are typical of hyperparathyroidism, but I do not want to make the diagnosis because she also had a large spleen and something wrong with the blood. There are several red herrings in this case, such as the mass in the chest. It may have been a thymoma, but so far as I know, they never give a syndrome like this. It may have been thyroid or parathyroid tu-

mor. We assume it was pushing the esophagus over, and I do not believe a parathyroid tumor would have done that. It may have been Hodgkin's disease or a tumor of the lymphoma series, but the picture does not correspond to generalized reticulum-cell sarcoma because it lasted too long. This bone lesion could be a lipoid dystrophy like Gaucher's disease. May I ask whether there were yellow spots on the scleras, especially toward the inner canthi.

DR. HARRY F. KLINEFELTER: No, there were no pingueculae.

DR. AUB: The patient was fifty-seven years old. Gaucher's disease would give her many of the things she had, but I have never heard of its producing a high blood calcium and a low blood phosphorus. It would give bone lesions. It could give a moth-eaten appearance like the x-ray picture in the phalanges and the thickened bones of the femurs. It would produce the large spleen, the anemia and the low white-cell count, and could explain all these things and bring the picture together, except for the high blood calcium and low phosphorus. On the whole, I think one of the xanthomas—of which Gaucher's disease would be the likeliest, because of the age—would explain the low cholesterol, and everything else would go with it; I do not believe this woman had cancer. I am quite sure that she did not have multiple myeloma. I do not believe she had lymphoma, and I am unwilling to make a diagnosis of hyperparathyroidism. I do not believe that Gaucher's disease is a good diagnosis, but it is the diagnosis that explains most of the findings and I am therefore willing to make it.

DR. TRACY B. MALLORY: Dr. Schatzki, do you want to comment on the possibility of Gaucher's disease as an explanation of the bone lesions?

DR. SCHATZKI: The spleens in Gaucher's disease are usually larger than the spleen in this case.

DR. AUB: Yes; much larger, and there ought to be little xanthomas in the eyes, which this patient apparently did not have.

DR. SCHATZKI: From the roentgenologic point of view, this is not Gaucher's disease. Cases with Gaucher's disease do not show real cysts.

DR. ALBRIGHT: I think they do not have cysts and are very radiosensitive.

DR. AUB: In Gaucher's disease? No.

DR. ALBRIGHT: Yes.

DR. MALLORY: The authorities seem to disagree.

DR. SCHATZKI: Gaucher's disease does not produce decalcification of the feet.

DR. AUB: No, it does not.

DR. SCHATZKI: One thing is wrong with the description in the abstract so far as the x-ray film is concerned: except for the skull there is no thick-

ening of the cortex of the bones. The cortex of the femur is normal, and that of the humeri, radii and ulnae is definitely thin.

DR AUB: The patient had an elevated calcium output. Should you make a diagnosis of hyperparathyroidism on that femur?

DR. SCHATZKI: I should not rule it out by any means. The femur alone shows the cysts. There are cysts and a thin moth-eaten appearance. I think that is all right.

DR AUB: I think it may be xanthoma. However, if you want to ask me what operation should be done, I should operate and take a biopsy of the bone.

DR EDWARD D. CHURCHILL: You are not advising a splenectomy or mediastinal exploration or a neck-cervical exploration for parathyroidism?

DR AUB: I strongly suspect that you did look at the lesion in the chest, but I should have had a biopsy of the bone first. Did you do a biopsy?

DR OLIVER COPE: Yes.

DR AUB: Of what?

DR COPE: A biopsy of the ilium.

CLINICAL DIAGNOSIS

Hyperparathyroidism

DR AUB'S DIAGNOSIS

Grucher's disease

ANATOMICAL DIAGNOSES

Osteitis fibrosa cystica

Adenoma of the parathyroid

Neurofibroma of mediastinum

PATHOLOGICAL DISCUSSION

DR MALLORY: The wall of one of the cystic cavities in the ilium was chiseled off. The cyst contained material resembling a benign giant cell tumor, and its bony margins were characteristic of osteitis fibrosa.

DR AUB: Then, it is obvious that the patient must have had a parathyroid tumor. I do not understand why you x-rayed this woman so hard.

DR MALLORY: I suggest we defer discussion on that point until Dr Cope has told us about the second operation.

DR COPE: We had an amusing time arguing about this diagnosis because none of us was exactly right. Dr Albright and I thought the tumor mass seen by x-ray study must be parathyroid. Dr J. H. Means was on service and thought it was not, arguing that it was too low and too large and that it must be thyroid tissue in the mediastinum. But we have seen one parathyroid adenoma in our series that was as large as this. As a mat-

ter of fact, the adenoma from the first case we had weighed 53 gm., and one other patient had one almost as large. Chemically, the patient under discussion had an endocrine disease,—hyperfunction of the parathyroid hormone,—and when a tumor mass is demonstrated on physical or x-ray examination, the burden of proof is on him who says that the tumor is not the cause of the disease. X-ray treatment was decided on because this seemed the case par excellence to prove the inefficiency of such therapy. Not knowing exactly where the tumor was in the other 5 patients who had received such treatment, we were never sure that the irradiation had reached the tumor. I was therefore in full sympathy with having this tumor irradiated.

We divided the sternum at operation down the midline, and as I put my finger in to go underneath and push the pleura away from the under surface of the sternum, I felt ahead of my finger a soft, small tumor. It was not in the place of the large tumor, but higher up. By great good fortune for the patient, the actual parathyroid tumor

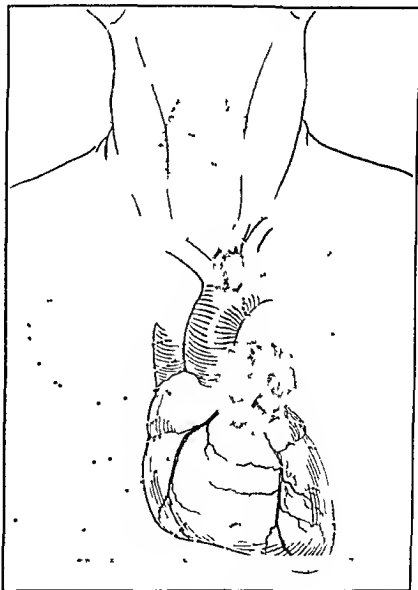


FIGURE 2

was also in the anterior mediastinum. Its shadow in the x-ray film is probably this one just above the larger tumor. This is a photograph of the two tumors removed at operation, placed on a drawing of the chest and neck (Fig 2). The parathyroid

tumor was within the thymic capsule, and this lighter colored tissue attached to it is a piece of the normal thymus gland. This patient is one of the roughly 10 per cent of people with hyperparathyroidism whose tumor lies in the anterior mediastinum instead of in the neck. It was good fortune because we did not explore her neck first, and if the tumor had not been in the mediastinum we should have had to explore her neck at a second operation.

We had an amusing time with the pathologists too. I had already taken out the parathyroid gland,—I thought it was parathyroid,—but it was quite green; Dr. Castleman looked at it and said, "Well, I am not sure of that." Dr. Churchill, on the other hand, was quite sure it was parathyroid. We were all agreed about the larger tumor, which was hard and firm and looked like a thyroid tumor.

DR. SCHATZKI: Dr. Albright prompted us to treat the patient because the literature contains numerous reports of beneficial results from treating parathyroid tumors with x-rays. He thought we could see the tumor, and if it shrank we should have definite proof that it was radiosensitive. It did not change in size, however.

DR. ALBRIGHT: I wanted to prove the fallacy of x-ray treatment once and for all.

DR. MALLORY: Microscopic sections of the tumors eventually proved that the smaller mass was a parathyroid adenoma and the larger one a mediastinal neurofibroma. Its presence must be regarded as pure coincidence, and it obviously had nothing to do with any of the symptomatology.

DR. COPE: The color interested me. The parathyroid tumor was brown when I first exposed it within the thymic capsule, but I divided its arterial blood supply. Ordinarily, when we excise a parathyroid tumor, we take the entire pedicle out with one snap, so that the blood is retained within the adenoma. This time, the arterial supply came from above, and the main venous return was from below. I divided the arterial supply first, and all the blood had drained before the veins were severed. With the loss of blood, the tumor turned a curious green. I realized on looking back that I had seen this happen before but had never made proper note of it.

DR. WILLIAM B. BREED: We still have not settled the low phosphatase.

DR. AUB: Did the phosphatase go up?

DR. COPE: Two months after operation, it had gone up. We have not seen the patient since April 18. Immediately after operation she showed the expected changes. The calcium came down promptly. The phosphorus did not go lower, but started up the first week after operation. Had

there been any amount of osteoblastic tissue that should have been associated with a high phosphatase level, we should have expected the phosphorus to go down rather than up in the initial postoperative period.

DR. AUB: What about the large spleen?

DR. MALLORY: It could have been hematopoietic. After all, the patient had a considerable portion of bone marrow replaced by fibrous tissue.

DR. AUB: That is uncommon with leukopenia, is it not?

DR. ALBRIGHT: We had another case with equally bad anemia without a large spleen.

CASE 28312

PRESENTATION OF CASE

A twelve-year-old boy was admitted to the hospital because of repeated fractures of the arm.

When a baby, the patient broke his right wrist. Four years before entry, and again two years before entry, he fractured his left arm. Two weeks before entry, the left arm was broken for a third time, in a fall against a curb while the patient was walking. The roentgenogram taken the day after the accident at another hospital showed a fracture of the humerus, and the patient was transferred to this hospital for treatment.

Examination showed a well-nourished and well-developed boy, with normal chest and abdomen. The arms were of equal length, without local swelling, heat or roughness. Tenderness was noted over the medial epicondyle and upper third of the shaft of the left humerus.

The temperature, pulse and respirations were normal.

Examination of the blood showed a white-cell count of 7300 with 70 per cent polymorphonuclears, 20 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosinophils. The blood Hinton reaction was negative. The serum calcium was 11.7 mg., the phosphorus 4.6 mg. and the phosphatase 7.2 Bodansky units per 100 cc.

A roentgenogram of the left arm showed absence of normal trabeculation of the upper two thirds of the humerus, and thinning of the cortex of the upper quarter (Fig. 1). The medullary cavity was crossed by irregular scattered calcified trabeculae giving the pattern of irregular cysts. There was a fracture of the cortex of the medial aspect of the humerus about 1 cm. below the upper epiphyseal line, apparently involving the wall of a cyst, with a fragment of cortex lying transversely across the bone. The upper humerus seemed questionably expanded. No definite soft-tissue mass was visible. The process did not cross the epiphyseal line.

Roentgenograms of the right arm, right thigh and left forearm showed no abnormalities

On the tenth hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR ERNEST M. DALANO: We are dealing here with a boy of twelve who had three fractures through the same bone, and this last fracture was apparently due to a very trivial blow. It suggests



FIGURE 1

an underlying pathologic condition of the humerus. We must consider three things: simple bone cyst, giant-cell tumor, and a cyst from a generalized process such as osteitis fibrosa cystica, in which there are apt to be many cysts on an underlying parathyroid basis.

I called attention to the fact that there seemed to be no bowing, and in a cyst of the parathyroid type, osteitis fibrosa cystica, there is quite likely to be deformity of the bone and bowing. It is suggested here definitely that there has been a fracture three times through this same cyst, and yet we still have a normal contour of the arm. In review-

ing the x ray films, it is evident that other bones have been examined to rule out the possibility of a generalized fibrous cystica disease. These were reported to be normal and seem to be normal. The serum calcium and phosphorus are high normals,—about what one would expect in a boy of twelve. The phosphatase is normal for a child. I believe, on these grounds, we can rule out osteitis fibrosa cystica, so that the differential diagnosis lies between bone cyst and giant-cell tumor.

The one lesion lies in the upper end of the shaft of the humerus. The note has been made that the condition does not cross the epiphyseal line. That is quite important because a giant cell tumor at the end of the bone will cross the epiphyseal line, extend all the way to the cartilage of the joint but not cross the joint, destroying everything up to the cartilage. This boy, however, showed a process that stopped exactly at the epiphyseal line. The typical giant-cell tumor is, moreover, an expansile type of tumor, so that the tumor itself is roughly spherical. It would not tend to spread down the shaft so far as this has without widening to a greater degree the bone at the upper end of the shaft. Another characteristic of a giant-cell tumor is that at the lower margin where it tends to go down into the shaft, a saucerlike depression is seen in the films and is also easily demonstrable on the operating table. That is quite typical, and I do not see anything suggesting it here. Other types of tumor involving the medulla tend to diffuse out and disappear gradually down into the medulla. I think this is more suggestive of bone cyst because of its lack of great widening, the lack of spherical tendency and the failure to cross the epiphyseal line. The patient had a trivial fracture, which brought him to the hospital. It is quite typical of patients with bone cyst that a fracture first calls it to their attention. There is a tendency for some of these bone cysts to heal spontaneously, once fractured. This boy had two opportunities, apparently, for spontaneous healing after fracture, but the tumor still persisted. If healing does not occur spontaneously, or as the result of operation, there is a tendency toward extension and further cystic degeneration.

My opinion is that this was simple bone cyst, benign, limited to the one bone and with a fracture. The usual method of handling these cases in this hospital is to open into the cyst and curette out the contents and then fill up the cavity with bone chips or osteoperiosteal grafts. Ordinarily, they heal and give satisfactory regression.

DR LAURENCE L. ROBBINS: I think the description of these x ray films is adequate. The appearance is more that of a cystic lesion than of a giant-

cell tumor. It has sometimes been said, and particularly stressed by Dr. M. C. Sosman, that giant-cell tumor never appears until after an epiphyseal line is closed and that it always involves the end of a bone. Atypical cases, which have been called giant-cell tumors on histologic examination, have not crossed the epiphyseal line. This, however, is a fairly characteristic picture of a cystic lesion of a bone.

DR. CHANNING C. SIMMONS: Did the skin in this case show any evidence of pigmented areas?

DR. TRACY B. MALLORY: No.

Have you anything to add, Dr. Smith-Petersen?

DR. MARIUS N. SMITH-PETERSEN: No, except that I am surprised to hear Dr. Daland mention the possibility of giant-cell tumor in a boy of twelve.

DR. DALAND: *Geschickter** has reported several at this age.

DR. SMITH-PETERSEN: About how many turned out to be cysts? Have you seen many at twelve, Dr. Simmons?

DR. SIMMONS: I have seen one case of epiphyseal chondromatous giant-cell tumor. That one crossed the epiphyseal line in a child of thirteen, as I remember.

DR. MALLORY: What about the relative frequency of spontaneous pain in bone cyst as against giant-cell tumor?

DR. SMITH-PETERSEN: I do not believe there would be any difference.

CLINICAL DIAGNOSIS

Bone cyst, left humerus.

*Geschickter, C. F., and Copeland, M. M. *Tumors of Bone (Including the Jaws and Joints)*. Second edition. 832 pp. New York: American Journal of Cancer, 1936.

DR. DALAND'S DIAGNOSIS

Bone cyst (benign).

ANATOMICAL DIAGNOSIS

Bone cyst, left humerus.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was operated on, and a cyst found. The pathologic picture was complicated by extensive hemorrhage, a good deal of it quite fresh and probably secondary to the pathologic fracture. The material curetted out consisted of edematous fibrous tissue, with fresh and old blood in it. No giant cells were found, and nothing that would suggest giant-cell tumor from a histologic point of view.

Would you care to say anything about treatment?

DR. SMITH-PETERSEN: No, except that frequently a little part of the cyst remains and keeps on growing. I think one is apt to be a little too optimistic about the results of packing in bone chips.

DR. DALAND: Was the appearance of this mass that was curetted different from giant-cell tumor? Grossly, could you tell the difference?

DR. MALLORY: I am not at all sure that I could. The cavity was quite well filled with semisolid, deeply blood-stained material. It was not a frankly cystic cavity, but I think the hemorrhage and the complication of fracture were partly responsible for that.

DR. DALAND: Was this found to be one large cystic cavity at operation?

DR. MALLORY: Yes, so far as the operator could make out.

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MASSACHUSETTS MEDICAL SERVICE

EVERY licensed physician in Massachusetts will receive by mail this week a brochure describing in detail the methods of operation of the Massachusetts Medical Service, the state wide system for prepaid budgeting of medical care sponsored by the Massachusetts Medical Society. This corporation, popularly called the BLUE SHIELD, will offer protection to employees and their families against the financial burdens of severe illness. As many physicians know, it is the fruit of more than three years' study by a special committee appointed by the Society and is based on the opinions of the best thinking medical men throughout the country. It is, in effect, the physicians' own answer to the grave social problem confronting the Nation

of how best to provide adequate distribution of medical care, and those who have studied the problem believe that this plan is far sounder than the schemes that have been and are being advanced by governmental, state and consumer-co-operative groups.

The present contract will offer hospital surgery, obstetrics and diagnostic x-ray services. It is the initial step in the development of a complete medical service and is limited in scope only because the public is not yet ready for a full coverage contract. The limitations of the contract, however, do not exclude any physician from participation, and every doctor is urged to participate from the outset of the plan, which will next develop a contract covering all hospital expenses and, finally, one including medical expenses in hospital, home and office.

The Blue Shield is an actuality; its charter has been granted, its capital funds have been provided by the Massachusetts Medical Society, and its offices are open at 230 Congress Street, Boston. It has joined forces with the Blue Cross and will reap the benefits of the hospital plan's wide backing by industrial and business leaders, as well as the confidence of its more than 400,000 subscribers. The Blue Cross will take over the administrative functions and the enrollment of subscribers for the Blue Shield, but each will act as an independent organization, with the allocation of costs subject to the approval of the State Commissioner of Insurance. This arrangement will save duplication of effort, needless expenditure of funds and serious loss of time.

Field representatives will begin calling on physicians this week, immediately after the mailing of the Blue Shield brochure. Obviously, they cannot interview the more than 7000 registered physicians in Massachusetts, and it is hoped that the brochure will explain all the details of the plan so amply that many physicians will sign the contracts without having been interviewed and will return them at once to headquarters.

The tempo of the times is swift, and the social problem that the new plan can solve is pressing. The Blue Shield has announced that it will be

ready for the public, with the Massachusetts medical profession solidly behind it, shortly after Labor Day. This goal can be achieved only if *every* physician in the State makes it his individual responsibility.

INDUSTRIAL MEDICINE FOR PRACTITIONERS

THE precipitous current events in the world at large can leave no lingering doubts in the mind of any group or individual that now is the time to "pick up the ball and run": one should not postpone adjustments, inconveniences or sacrifices that will contribute to the preservation of the Nation. The medical profession is fortunately placed in being able to contribute to this purpose in many ways: the younger members of the profession are being called to posts of active military duty; many of the older physicians are returning to hospital and teaching staffs and even to private practice; and the middle-aged doctors—most of whom served in the last war—are experiencing no difficulty in finding opportunities to apply themselves and their skills in all sorts of civilian activities.

Although the members of this middle-aged group are, or soon will be, carrying the heaviest practical burden, they are probably more goaded than other physicians by their inability to participate in a more direct way than that permitted by their physiologic limitations. They are partially compensated by serving on various boards and committees and by more extended tours of practice, but as they find their medical journals devoting more and more space to the military aspects of medicine and surgery, and when they glance at the headlines of the daily press, they must be frequently plagued by their inability to express themselves more concretely in the war effort.

How can these middle-aged physicians remaining in civilian practice intensify their influence in the total drive against impending disaster? A partial answer for many, and a complete answer for some, may be found in the cultivation of an interest in industrial health in their towns and

neighborhoods. In Massachusetts, three quarters of the industrial workers are employed by small companies. To date, the development of modern industrial medicine has been chiefly confined to the large plants, with their more serious problems and greater resources; as a result, its application to each and all the hundreds of little shops has been overlooked. Yet many of these small factories are now open night and day, thus exposing thousands of workers to hazards against which they might be very easily protected.

Who is going to cast a preventive eye on this widely dispersed problem? Who could do it more effectively than the local physician—the doctor who is asked to remove the foreign bodies, to suture the lacerations, to soothe the irritated skins, to x-ray the broken bones, to assuage the gastrointestinal disturbances and to calm the paranoid grievances of the more unstable but nevertheless productive workers? Here is a great untilled field—untilled because it does not lend itself to the wholesale methods that have brought such good results in the larger plants. The acreage is subdivided into hundreds of small plots, each of which must be worked by the hand of the local doctor, who can make himself see the possibilities of industrial-accident prevention as plainly as he saw those of diphtheria prevention twenty years ago.

If the local physician needs assistance in this matter, it is already within his reach. For a beginning, he may heed the announcement of the Committee on Industrial Health in this issue of the *Journal*. In the pamphlet there referred to, he will find a series of references and agencies that can help him. He may consult the *Manual of Industrial Health*, which will soon be issued by the Council on Industrial Health of the American Medical Association. He may subscribe to *Industrial Medicine*, the official monthly publication of the American Association of Industrial Physicians and Surgeons. Primarily, however, he should visit the plant or plants where he is occasionally called to serve, and he should do so with a trained, critical and inquisitive eye. Only in this way can he

accomplish results, and only in this way can he attract the attention of employers and the more intelligent employees to these results.

The alignment of all plants and factories, regardless of their size, to the modern practice of industrial medicine and hygiene would be a stupendous contribution to the war effort; and its accomplishment is clearly the opportunity of the middle-aged physician who remains in civilian practice.

OBITUARY

WALTER JOSEPH LAMARCHE

1859-1942

The death of Dr. Walter J. LaMarche on May 30, 1942, after a short illness calls for recognition. He was in his eighty-third year and had practiced medicine in Cambridge for fifty years, where his kindly manner and personal interest in his patients earned him their respect, friendliness and loyalty. His interest and his care were as sincere and genuine in his visits to the hopeless and incurable at the Holy Ghost Hospital for Incurables, which he served many years, as it was with his private patients, who offered a more hopeful prognosis and gave more inspiration—a test that many of us find hard to meet. He was for several years identified with the Orthopedic Department of the Massachusetts General Hospital and faithfully gave to it his time and attention.

He had been a pupil of Pasteur in Paris; his command of the French language helped him to a personal touch with the great scientist, and at times with his friends, almost always after a little urging, he would reminisce thereof. Dr. LaMarche was popular among the profession and invariably courteous to his confreres. He will be greatly missed by his many patients, of both short and long tenure, who benefited by his constant kindness and understanding.

Requiescat in pace.

A. W. D.

MEDICAL EPONYM

PROFETA'S LAW

This law was enunciated by Dr. Giuseppe Profeta (1840-1910), of Palermo, in an article, "Sulla Sifilide per Allattamento [Syphilis from Nursing]," that appeared in *Lo Sperimentale* (IV series 15: 328-338 and 339-418, 1865). A portion of the translation follows:

Thus, the healthy child born of a syphilitic mother may with impunity take the breast of its own mother or that of a syphilitic nurse, and neither the milk nor the presence of infectious lesions on the breast of the mother or the wet nurse is capable of transmitting the disease.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON INDUSTRIAL HEALTH

The Committee on Industrial Health calls the attention of the fellows of the Society to a pamphlet, *Manual on Industrial Health for Defense*, which has been prepared by the Division of Health and Social Services, Massachusetts Committee on Public Safety, and is being distributed this week to all practicing physicians within the Commonwealth by the Massachusetts Department of Public Health. It should be especially suggestive and of interest to those physicians who work for a few hours daily, or only in a casual way, caring for industrially connected illnesses and accidents. The Committee on Industrial Health bespeaks the attention of all such physicians for this little publication.

DWIGHT O'HARA, *Chairman*

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY: OPERATIVE DELIVERY FOLLOWED BY SHOCK AND DEATH

A twenty-eight-year-old primipara had been seen routinely during her pregnancy and had had adequate care. At the beginning of pregnancy, a blood Wassermann reaction had been reported positive, and in consequence of this, thirty injections of bismuth had been given; the Wassermann reaction at the end of pregnancy was said to have been negative. At this time, the systolic blood pressure rose to 130, and there was a trace of albumin in the urine. Labor started three days after spontaneous rupture of the membranes and lasted forty-one hours. Then, primary inertia of the uterus developed, and as full dilatation existed, forceps delivery was attempted. In spite of the fact that the head was low, delivery was so difficult that the fetus was decapitated, and extraction of the shoulders was accomplished only with great effort. The placenta was said to have been adherent, and was extracted manually. The patient died shortly afterward.

Comment. It is regrettable that any patient who had such intelligent and adequate care during the prenatal period should have been so mishandled at the time of delivery. It is, of course, possible that a so-called "dry uterus" resulted in a con-

traction ring and that this may have been the sole cause of difficulty. Or, if a contraction ring did exist, which seems likely, death may have been due to rupture of the uterus.

Intelligent obstetric management during labor would have obviated this maternal fatality. There is some question in the history regarding just when the death of the fetus occurred, but it apparently died during labor. If so, intelligent obstetrics should also have averted this disaster. Such bungling obstetric operating today is hardly understandable and certainly not to be condoned.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JUNE, 1942

DISEASES	JUNE 1942	JUNE 1941	FIVE-YEAR AVERAGE*
Anterior poliomyelitis	0	1	6
Chicken pox	1265	1170	1134
Diphtheria	14	11	9
Dog bite	1414	1265	1370
Dysentery, bacillary	2	14	13
German measles	1328	535	181
Gonorrhea	355	302	364
Measles	3654	3923	3527
Meningitis, meningococcal	19	16	8
Meningitis, other forms	10	—	—
Mumps	1325	1113	719
Paratyphoid infections	8	5	14
Pneumonia, lobar	160	207	242
Scarlet fever	793	639	669
Syphilis	512	391	424
Tuberculosis, pulmonary	342	264	293
Tuberculosis, other forms	26	22	33
Typhoid fever	4	7	6
Undulant fever	3	6	5
Whooping cough	951	978	717

*Based on figures for preceding five years

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES June, 1942

Diphtheria was reported from: Boston, 1; Boylston, 1; Cambridge, 1; Fall River, 8; Medford, 2; Wrentham, 1; total, 14.

Dysentery, bacillary, was reported from: Beverly, 1; Waltham, 1; total, 2.

Encephalitis, infectious, was reported from: Leicester, 1; New Bedford, 2; Quincy, 1; Springfield, 1; Wellesley, 1; total, 6.

Malaria was reported from: Camp Edwards, 1; total, 1.

Meningitis, meningococcal, was reported from: Amesbury, 1; Beverly, 1; Boston, 3; Brockton, 1; Cambridge, 3; Chelsea, 1; Fort Banks, 1; Haverhill, 1; Hopkinton, 2; Medford, 1; Newton, 1; Peabody, 1; Taunton, 1; Wilmington, 1; total, 19.

Meningitis, other forms, was reported from: Beverly, 1; Boston, 2; Brockton, 2; Cambridge, 1; Dedham, 1; Foxboro, 1; Leominster, 1; Malden, 1; total, 10.

Paratyphoid infections were reported from: Boston, 1; Ludlow, 1; Medford, 1; Salem, 4; Watertown, 1; total, 8.

Septic sore throat was reported from: Barre, 2; Boston, 3; Cambridge, 1; Canton, 1; Malden, 1; Newton, 1; Waltham, 2; Winchendon, 1; Winchester, 2; Worcester, 1; total, 15.

Trichinosis was reported from: Stoneham, 1; Belcher town, 1; total, 2.

Typhoid fever was reported from: Fall River, 1; Woburn, 1; Worcester, 2; total, 4.

Undulant fever was reported from: North Andover, 1; Spencer, 1; Wilbraham, 1; total, 3.

Communicable diseases reported at figures above their respective five-year-average incidences included chicken pox, diphtheria, dog bite, scarlet fever, measles, German measles, syphilis, pulmonary tuberculosis, meningococcal meningitis and whooping cough.

Mumps was reported at a record-high figure for the tenth time during the past eleven months.

Anterior poliomyelitis reached a record-low figure with no new cases reported this month, for the first time since the disease was made reportable.

Reported at figures below their respective five-year incidences were bacillary dysentery, gonorrhea, paratyphoid infections, lobar pneumonia, tuberculosis (other forms), typhoid fever and undulant fever.

Cases of animal rabies were reported from Woburn and Attleboro, the former maintaining an old focus and the latter starting a new focus in the southeastern section of the State.

NOTES

The following promotions on the faculty and teaching staff of Harvard Medical School, effective July 1, were recently announced: George Van S. Smith, W. H. Baker Professor of Gynecology; Francis R. Dieuaide, clinical professor of medicine; Edward W. Dempsey, assistant professor of anatomy; Robert N. Nye, assistant professor of bacteriology and immunology; Austin M. Brues, assistant professor of medicine; Robert E. Gross, assistant professor of surgery; Frank W. Maurer, assistant professor of physiology; Madeleine F. Warren, assistant professor of physiology; Wilfred W. Westerfeld, associate in biological chemistry; John H. Dingle, associate in medicine; Charles A. Janeway, associate in medicine; Nathan B. Talbot, associate in pediatrics; Leslie Silverman, associate in industrial hygiene; and Joe V. Meigs, clinical professor of gynecology.

Dr. René Jules Dubos, member of the Rockefeller Institute for Medical Research, was recently appointed George Fabyan Professor of Comparative Pathology and professor of tropical medicine at Harvard Medical School. He succeeds Dr. Ernest E. Tyzzer, who becomes professor emeritus.

Dr. Eugene A. Stead, Jr., instructor in medicine at Harvard Medical School, was recently appointed head of the department of internal medicine at Emory University School of Medicine, Atlanta.

CORRESPONDENCE

SUSPENSION OF LICENSE

To the Editor: This is to inform you that at the meeting of the Board of Registration in Medicine held on July 17, 1942, the Board voted to suspend the license of Manford R. Spalding, 129 Central Street, Auburn, Massachusetts.

H. QUIMBY GALLUPE, M.D., *Secretary*

State House
Boston

REPORT OF MEETING

EVANS MEMORIAL LECTURE

At a Robert D Evans Memorial Lecture at the Evans Memorial, Massachusetts Memorial Hospitals, on March 27, Dr William Dock discussed Albuminuria and Associated Renal Changes.

In the many years between the original theories of Bright and the more recent observations of Addis, there has been little progress in this field. It was the keen observations of the little known Bestock, who did the actual urinalyses for Bright, that led to the latter's conclusions that albuminuria may result from many causes, most of them trifling, the albumin in the urine is that of the blood, the specific gravity of the urine is lower in drops, even in the presence of albuminuria, and albuminuria results in a lowered serum protein. These fundamental observations were not significantly enlarged on or their mechanism elucidated until various clearance tests and quantitative sediment studies were carried out recently by Addis.

It is still agreed that the causes of proteinuria are many and often trifling. Grossly, such kidneys are large, yellow and greasy. Microscopically, the tubules are full of fat. Originally, this substance was considered similar to that of the fatty degeneration of the brain, heart and liver, and this theory persisted until a few years ago. The glomeruli may look normal to the uninitiated but Bell in 1938, demonstrated that glomerular changes can be found in post mortem examinations of persons over twelve years of age. In 1931, Marshall et al showed from comparative studies on fish that proteinuria is dependent fundamentally on glomerular damage. Ekholm confirmed the belief that the basic proteinuria is glomerular and that the tubules of such kidneys are called on to reabsorb large quantities of protein. The glomerular filtrate in frogs contains a higher percentage than bladder urine in severe damage, and the tubular changes may therefore be secondary.

Heymans demonstrated the tubular reabsorption of trypan blue and even a sort of phagocytic action on large foreign particles like those of India ink. In searching for a protein with a good distinguishing tag on it, Whipple hit on the use of hemoglobin. Injecting this substance, he determined that it does not appear in the urine until the concentration is over 100 mg per 100 cc. If the concentration is greater, hemoglobin spills over like a threshold substance in proportion to the serum concentration, and hemosiderin is found in the tubules like trypan blue. Only 3 per cent of the hemoglobin is found in the glomerular filtrate, compared with 30 per cent for such crystalloids as sugar, and it crosses even normal glomeruli. By this method, a dyed protein can be studied, and it is found that this one is a threshold substance, in all respects like sugar, with large amounts filtered and reabsorbed until the value exceeds the threshold. The glycogen in the tubules of diabetes is similar to the stored protein in proteinuria except for the different parts in which they are absorbed.

Known functions of the kidney include an ultrafiltration by the glomeruli and a reabsorption by the tubules of colloids, fine precipitates, water and crystalloids. The tubules also have some excretory function, notably of Diodrast, which amounts to almost 100 per cent. They also form ammonia and store iron and glycogen. To study the role of the kidney in regard to protein, a dye called Evans's blue, which is taken up by protein, is used. This is passed by abnormal kidneys only, and then in proportion to the amount of protein. Even in the normal kidney,

a small amount of blue is noted in the tubules, although none is found in the urine. On the other hand, the tubules and urine are filled with the dye in proteinuria. This confirms the findings with hemoglobin and indicates that proteinuria is a result of glomerular dysfunction despite the fact that Richards et al have not been able to demonstrate the presence of protein in the glomerular filtrate.

But this method of microcannulation is inadequate to determine the small amount of protein expected. By perfusing of the kidneys with ice-cold serum, the material from the uterus is found to be identical with glomerular filtrate. Therefore, it is necessary merely to paralyze the tubules by this method and then remove the pelvic urine by ureteral catheterization. That no damage to the glomeruli results from this severe treatment is evident from the complete recovery of functions in animals that recover. By adding hemoglobin to the perfusion mixture, one can demonstrate that definite amounts of protein in about the concentration found in the cerebrospinal fluid can be collected (15 to 24 mg per 100 cc). The tubular reabsorption of fat and protein, therefore, is a normal phenomenon, and their presence in the tubules in large amounts is the result of overwork in an attempt to clear a heavily concentrated ultrafiltrate. It is not a true degeneration. The passage of protein in the urine occurs in inverse proportion to the size of the molecule, and it is too, is a glomerular function.

Clinically, there may be tubular paralysis allowing proteinuria similar to renal glycosuria. Table 1 indicates the average findings in certain renal conditions.

Early in renal disease, therefore, the tubules save the body a large amount of protein filtered by the glomeruli,

TABLE 1

CONDITION	GLOMERULAR FILTRATE			URINE		
	VOLUME l per 100	PROTEIN mg / cc	N day	VOLUME l per 100	PROTEIN mg / cc	N day
Normalcy	180	20	0.36	1.0	2	0.02
Mild nephritis	180	41	40	1.0	200	2.00
Severe nephritis	180	62	74.00	1.0	2000	20.00

but later they, too, leak. The threshold for protein seems to be about 40 mg per 100 cc in the normal and mildly diseased cases and 30 mg per 100 cc in the chronic and severe cases.

Tubular changes in proteinuria, therefore, are secondary. The tubules are overfed, not poisoned. Actual degeneration may also be present, especially in later stages of renal disease. The lipid tubular changes are the result of lipemia secondary to the low plasma protein. Why the glomerulus leaks has not yet been solved.

BOOK REVIEWS

The Medical Aspect of Boxing By Ernst Jokl, MD ⁸, cloth, 251 pp., with 55 illustrations and 4 plates. Pretoria South Africa J. L. Van Schaik, Limited, 1941 17s 6d.

This timely volume, devoted to a demonstration of the serious injuries sustained by professional boxers and, to some extent, amateurs as well, draws attention to matters very generally unknown and almost never discussed publicly.

The primary object is to prevent the known fatalities in the prize ring and their causes as revealed by autopsies and in other ways. The fatalities not occurring before the public and in the 'prize ring' are doubtless quite as numerous, for such occurrences would be likely to be ascribed to other causes, if reported at all.

In the professional field, boxing is the only sport in which the major competitive effort is directed to the adversary's head. The skull is more or less elastic and is of somewhat variable thickness in different persons. Hence, severe, individual blows on certain localities momentarily change the diameters of the cranial cavity; as a result, the soft contents may be so severely disrupted that serious hemorrhage occurs. This may be subdural or more deeply seated. Occasionally, there may be an actual skull fracture by *contrecoup*.

Aside from such tragedies, which are by no means unusual, statistics show that oft-repeated blows on the head result in a condition known as "punch drunk." This appears to be best explained by small multiple hemorrhages, scattered over and through the brain. About 5 per cent of all professional boxers suffer from it if they keep at the game long enough. Its symptoms are both physical and mental. Quite a considerable number of them require institutional treatment.

In addition to these major injuries, there are many others, some of which are nearly as serious.

The attitude of colleges and schools, athletic trainers and others concerning the value of boxing in courses of physical training was obtained through questionnaires and was rather illuminating in many ways. The brutalizing effect of the sport on certain of its professional exponents, as well as on the portion of the public that patronizes exhibitions, is emphasized.

The facts brought out by the author should give food for thought in wartime, when so many young men are being inducted into services in which boxing is regarded and encouraged as a desirable means of training. The book should have a wide circulation and careful consideration.

The Baker Memorial: A study of the first ten years of a unit for people of moderate means at the Massachusetts General Hospital. By Haven Emerson, M.D. 8°, cloth, 75 pp. New York: The Commonwealth Fund, 1941. 50c.

This is a carefully written survey of an institution unique in the annals of American medicine. The operation of the Baker Memorial has been a success, and after some misgivings, all physicians connected with it, as well as their patients, are nearly universal in approving the service rendered. Such an institution could be duplicated elsewhere in the country, but before doing so, as Dr. Emerson points out, many factors must be taken into consideration. Experience has shown that to be adequate in all respects, such a hospital must be an integral part of a large general hospital, must maintain a daily census of not less than 200 patients, and must have a bed-day rate of \$4.00 to \$6.00 and a capital investment of \$2,000,000; furthermore, the trustees must find an additional \$500,000 for an endowment fund to meet operating deficits in the first ten years. Any surplus should be used to improve service or reduce rates, the staff must submit to certain financial standards, and patients must be selected. Any community that wishes to provide a hospital for patients of moderate means will do well to consider with great care the report of the first ten years of the Baker Memorial.

The Story of Clinical Pulmonary Tuberculosis. By Lawrason Brown, M.D., 8°, cloth, 411 pp., with 1 portrait. Baltimore: Williams and Wilkins Company, 1941. \$2.75.

Few people are so well qualified to write the story of the evolution of clinical tuberculosis as the late Dr. Lawrason Brown. During his lifetime, he witnessed and contributed to the emergence of tuberculosis from a disease of despair to one in which early diagnosis could be estab-

lished with a high degree of certainty and treatment instituted on a rational and sound basis. Dr. Brown, more than anyone else, epitomized the scholar, the clinician, the teacher and the enthusiastic worker in the field of tuberculosis. It is therefore most fortunate that Mrs. Brown and a group of Saranac Lake physicians have painstakingly gone over his historical notes, compiled them in book form and handed them over for posterity as a monument to a truly great man; a debt of gratitude is due them.

The book, which is written in a very fluent and delightful story-telling style, can be read with equal enjoyment by the laity and the medical profession. The first four chapters describe visits to the tuberculosis experts of the period 1700 to 1900. In these chapters, the dramatic changes in the concepts of tuberculosis are given against the background of the Renaissance and the pulsating history of European events during that time. Part two of the book deals with Laennec and his successors and also considers the beginning of early diagnosis, early publications in Germany and Austria and the diffusion of knowledge in England, as well as a most complete and fascinating chapter on early diagnosis as it was developed in the United States. The chapter on diagnosis by x-ray methods was contributed by Dr. Homer L. Sampson, and the chapter on the development of surgical methods was written by that great pioneer in thoracic surgery, Dr. Edward W. Archibald, of Toronto. There are excellent sketches and sidelights on the life of Laennec and his writings on the story of the stethoscope and a description of early medical journals.

On the whole, this book constitutes the most comprehensive work on the history of pulmonary tuberculosis. Its story keeps the reader's interest from its very beginning to the end. This book will undoubtedly find its place among the best authoritative works on the history of medicine.

Biology of the Laboratory Mouse. By the staff of the Roscoe B. Jackson Memorial Laboratory. Edited by Dr. George B. Snell. 8°, cloth, 497 pp., with 172 illustrations and 37 tables. Philadelphia: The Blakiston Company, 1941. \$7.00.

The staff of the Roscoe B. Jackson Memorial Laboratory are to be congratulated on this very useful book. The editor makes the following significant comment in the preface:

"Because it deals with the mouse alone, this book presents a vertical cross-section of biological knowledge rather than the more usual horizontal cross-section. It contains information about one animal drawn from various branches of zoology, rather than information about one branch of zoology drawn from observation of a variety of animals."

There are thirteen chapters, which deal with the early embryology of the mouse, reproduction, histology, spontaneous neoplasms in mice, gene and chromosome mutations, the genetics of spontaneous tumor formation, the genetics of tumor transplantation, endocrine secretion and tumor formation, the milk influence in tumor formation, inbred and hybrid animals and their value in research, parasites, infectious diseases of mice, care and recording. The illustrations are many and good, the index is useful, and most valuable, perhaps, is the excellent bibliography at the end of each chapter. Every library should own a copy of this book, which deals with a mammal so widely used in all laboratories.

(Notices on page ix)

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THE IMPACT OF THE WAR ON THE VENEREAL-DISEASE PROBLEM*

RAYMOND A. VONDERLEHR, M.D.†

WASHINGTON

THROUGH all history, syphilis and gonorrhea have been destroyers of the efficiency of armed forces. The story is familiar. During World War I, 6,800,000 man-days were lost in the United States Army because of venereal disease—equivalent to a year's absence from the service of 19,000 men. Actually, the number of new infections with venereal disease in the Army exceeded by 100,000 the number of battle casualties. Furthermore, in the Navy and the Marine Corps, 687,000 days were lost from duty because of venereal disease.

Material progress has been made in the fight against the venereal diseases, even though they have remained a major cause of noneffectiveness among the armed forces since 1918. This statement can be made in spite of the high prevalence of venereal diseases demonstrated by the routine serologic examination of selectees during mobilization for the present war. In the first million men, approximately 45,000 were found to have serologic evidence of syphilis or clinical manifestations of the primary and secondary stages of this disease.¹ An additional 15,000 were estimated to have gonorrhea. The preliminary data available on examination of the second million selectees confirm these figures. It would be extremely helpful to have available comparative data on the prevalence of syphilis in the men mobilized during World War I. The serologic test for syphilis in 1917 was new, expensive and technically much less reliable than at present. It was therefore not utilized routinely in the examination of the selectees, and a comparison cannot be made.

It is essential, however, to review some of the progress that had been made in the control of syphilis and gonorrhea before the beginning of the recent mobilization, that we may compare, in

the future, the control problems of venereal disease at the beginning and the end of the current war. Surveys² of sources of treatment in forty areas throughout the United States, representative of all sections of the country, were completed by the United States Public Health Service in 1935. Approximately 25 per cent of the total population of the country dwelt in these areas. The returns on these surveys included reports from more than 97 per cent of the treatment sources in such areas. The data available indicated that syphilis might be expected to strike one person in ten at some time during his life.² A year ago, the most careful statistical studies utilizing the material available from the routine serologic examination of selectees showed that the chance of acquiring syphilis is about one in fifteen. Consequently, each person stood only half the chance of being infected with syphilis in 1941 that he did about ten years previously.

Massachusetts has taken first place many times in the syphilis-control program. It was first to require the reporting of syphilis as a communicable disease; first to provide serologic tests without cost; and first to distribute antisyphilitic drugs to private physicians. Its hospitals were encouraged early to start venereal-disease clinics. If Massachusetts were an island,—out of touch with infections from without,—it is probable that the control measures carried on so far would have been sufficient to reduce the prevalence of syphilis to the low prewar rate in Scandinavian countries.

In industry, great gains have been made in the solution of the syphilis problem. Prewar results of blood tests on applicants and employees in eighteen of the large plants of the E. I. du Pont de Nemours Company, for three periods since the beginning of their program against syphilis, provide an example. Tests made on 27,000 people by this company during 1934 and 1935 yielded a prevalence rate of 39 per thousand. The rate of 51,000

*Presented at the annual meeting of the Massachusetts Medical Society Boston, May 26, 1942

†Assistant Surgeon General, United States Public Health Service.

tests made in 1937-1938 was practically the same — 40 per thousand. But among 35,000 persons tested in 1940-1941, the rate dropped significantly — to 10 per thousand. Gehrmann,⁴ chief industrial surgeon of this company, is of the opinion that this reduction in the prevalence of syphilis in widely scattered industrial plants was due primarily to insistence on regular treatment of infected employees. Similar reductions have been described by the surgeons of many other industries.

Even in the southern States, where the prevalence of syphilis had almost reached the saturation point, progress was made when the disease was attacked vigorously. As an example, in Glynn County, Georgia, where the first mobile unit for the control of syphilis was provided, the syphilis prevalence rate among Negroes in 1937-1938, the first year of operation of the mobile unit, was 391 per thousand.⁵ In the early part of 1941, however, the rate had dropped to 23.4 per thousand. In 1937, not one clinic patient in Glynn County had received the minimum treatment of twenty injections each of an arsenical compound and of bismuth. By March, 1941, 46 per cent of all patients admitted to the mobile clinic with early syphilis had received this protection. Most significant of all, the Negro stillbirth rate in this county has been reduced from 100 to 44 per thousand live births since the beginning of the syphilis-control program.

The first significant reversal of the downward trend in the venereal-disease rates was recorded recently when the Surgeon General of the Army reported that the admission rate for all venereal disease for the whole Army for the calendar year 1940 was 42.5 per thousand as compared with 29.6 in 1939.⁶ This trend upward has usually occurred in time of war and should stimulate an all-out application of every modern method for the control of the venereal diseases, in both the armed and the civilian populations. Provisions for early diagnosis and facilities for the institution of prompt treatment now exist in almost all areas with full-time local health services. The scarcity of trained personnel has handicapped the follow-up program, and some intelligence and ingenuity will be required to maintain the work at a satisfactory level. It may well be, however, that the solution of the war-time venereal-disease problem lies in individual prophylaxis. We must, as Lahey⁷ recommends, attempt to educate men to avoid venereal disease, but we must likewise understand that if this cannot be accomplished the necessity for prophylaxis must be promoted "even if it seems compromising to a sentiment." Today, as we are forced to spread even more thinly our supply of medically trained personnel, we must

not ignore the possibility of reducing case loads by taking every reasonable opportunity to prevent infections altogether.

One of the shocking revelations in the prostitution racket of recent years has been the participation of private physicians in the plunder. Time and again, where tolerated prostitution exists, the people in the community are given a false sense of security by being told that the prostitutes are rendered safe from venereal infections because they are subjected to periodic physical examinations. Much too frequently, reputable members of the medical profession perform these perfunctory examinations, and the prominence of the physician often lends support to the erroneous belief that this system is effective.

One among many instances can be cited that exemplifies the deplorable, yet profitable, part that private physicians have played in tolerated prostitution. Recently, the mayor of a city of about 50,000 openly supported a segregated area in which were located between 200 and 300 prostitutes. Nearby, the Army had concentrated men approximately equal to the total population of the town. The segregated district was doing a tremendous business, and the usual arguments against prostitution did not force the mayor to yield. He contended that the women in the area were examined periodically and were not the source of venereal diseases in the armed forces, although the Army rates were unusually high. Further investigation showed that the son of the mayor was a physician in private practice who was examining weekly the women in the segregated area at fees ranging from \$3.00 to \$5.00. It was not until the governor of the state brought pressure to bear on the mayor and his son that they could be persuaded to discontinue their support of the segregated area. The son, incidentally, was a reputable physician in the community and a member of the usual medical societies. Can we, as physicians, expect the public to take aggressive action against prostitution when some of the members of our own profession support the racket so flagrantly?

The routine serologic examination of selectees has produced a most serious problem of treatment and follow-up for infected men, who at the present time are excluded from military service. The record shows that serologic or clinical evidence of syphilis exists in approximately 45,000 of each million selectees examined under the Selective Service System. This rate holds true for the first and the second million, and it is estimated that within the next year 200,000 men with evidence of syphilis will have been discovered and excluded from military service. It is the obligation of the health officer and the physician in private practice to rehabilitate these syphilitic selectees.

Records showing the number of infected selectees brought under treatment throughout the United States are as yet incomplete. Steps are being taken to obtain better information as soon as possible. Present data available to the Public Health Service, however, show that on an average only half the infected selectees in the United States are being brought to treatment, and the percentage varies greatly in different sections of the country, depending on the existence of full-time local health services and a control problem for venereal disease well integrated with the local selective-service board. In many places with aggressive and efficient health officers, 100 per cent of the selectees are brought to treatment with the assistance of interested local selective-service boards. Other health departments do not do so well. When no health service is available, the entire responsibility for the treatment of infected selectees falls on the medical profession, and in such places, often only a very small fraction of the total infected selectees are brought in for examination and treatment. If during the next few years the numerous syphilitic selectees discovered through wartime examinations are given adequate treatment for their infections, one of the greatest accomplishments yet attained in the control of syphilis will have been made. If this opportunity is lost, however, it will constitute one of the greatest public-health and medical failures in the history of the United States.

In terms of relative prevalence, gonorrhea is four to eight times as common in the armed forces as syphilis. Comparative rates are not available for the civilian population, but it is quite probable that gonorrhea occurs there in much the same ratio. It is most discouraging that all health officers and physicians are not taking advantage of the modern

methods for the treatment and control of gonorrhea. Studies by the American Neisserian Medical Society, a great organization originally planned by the members of the Massachusetts Neisserian Medical Society, in co-operation with the United States Public Health Service, prove conclusively that there is no reason whatever for the high prevalence of gonorrhea if we will but apply present-day knowledge. Every man and woman with gonorrhea should receive the routine scheme of treatment recommended by the Executive Committee of the American Neisserian Medical Society.⁸

* * *

In all history, war has opened the gates to pestilence. Venereal disease strikes first, and its wounds are often the last to heal. At the present time, the United States is better prepared than ever before to wage an effective campaign against gonorrhea and syphilis. Tolerated prostitution and failure to apply promptly modern medical knowledge are the most vulnerable points in this field of medicine. Will the people of our democracy follow through against the venereal-disease foe within as efficiently as we will wage war against our enemies from without?

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MASSACHUSETTS PUBLIC-HEALTH PROBLEMS IN WARTIME*

PAUL J. JAKMAUH, M.D.†

BOSTON

WARTIME demands on public-health services are compelling in their urgency. A people fighting for its existence scrutinizes each new activity with but a single thought in mind: will this add to our combined strength and further our effort in the ordeal that confronts us? Slowly but surely, we are coming to the realization that, remote as this present world conflict appeared at first, it has become a stark reality in the daily life of every one of us. Our present national responsibility is enormous. The responsibility of those of us engaged in public health is equally grave.

Under normal conditions, a critical appraisal of current activity and of new developments is a deserving procedure in any well-regulated health department. An evaluation of recent developments is particularly appropriate at this time. When existing resources are being taxed to the utmost, when so large a part of our national wealth is being devoted to the war effort, when increasingly severe burdens are being heaped onto our economic structure, it is extremely necessary that each new undertaking be examined in minute detail. In assuming new responsibility, our professional personnel must be utilized in the most efficient manner. Emphasis must be placed on those services most intimately and directly concerned with our national security. Our entire public-health program must comply with this ideal to ensure its permanency.

During wartime, increased attention must be given in public-health programs to those groups in the general population who bear the brunt of the burden. After a critical review of the high percentage of rejections for physical defects among young men examined under the Selective Service Act, we come to a realization of the need for increased health service for the youth of our nation. I say this although I realize that, to some extent, this high percentage of rejections is due to higher health standards for the acceptance of selectees than those in World War I.

Although it is true that many of the defects date back to inadequacies having their origin during infancy and early childhood, it is evident that increasing emphasis must be placed on the pres-

ervation of health during later childhood and adolescence.

No one can foretell the duration of this war. The high-school student of today may be the soldier of tomorrow. In industry, young girls in large numbers will take on themselves the responsibilities formerly assumed by men. The increase in tuberculosis among young women already noted in England is a warning that should not be allowed to go unheeded. Our present public-health program must include measures that will safeguard in every possible way all our people, with particular emphasis on those who are directly engaged in war efforts of one type or another.

Before outlining actual developments, I shall make several generalizations concerning the relation of the Massachusetts Department of Public Health to health authorities at various other levels. The department stands midway between local and national health organizations. In most of its functions, it acts as an advisory and investigative body. Actual legal health authority is most frequently vested in local boards of health, this being a natural development of local autonomy, the fundamental political concept in Massachusetts. Similarly, federal authority has been limited by the Constitution to certain specifically designated powers beyond which it is essentially advisory in character. With the passage of time, more specific duties have been delegated to health authorities at the federal and state levels.

During the last decade, this nation has been passing through a period of intense social reform. It is difficult to comprehend the vast transformation wrought by the Social Security Act. Titles V and VI of this act have had a profound influence on public-health practice throughout the entire country. State budgets have been augmented by federal funds. Existing services have been improved, and new ones added, according to definite stipulations by federal authorities regarding the manner in which this money may be expended. Title V funds pertain to maternal and child-health services and the crippled-children's program, and are under the supervision of the Children's Bureau of the United States Department of Labor. Title VI funds, which are for general public-health administration, are under the supervision of the United States Public Health Service.

As this nation passes from a peacetime to a wartime footing, the tendency for federal subsidi-

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†Commissioner of Public Health, Massachusetts Department of Public Health.

zation has become more marked. The proposed plan for rehabilitation of men rejected by selective service boards and the contemplated establishment of medical and public health services in federal housing projects indicate the interest that federal agencies are paying to state and local health problems. Bearing these considerations in mind, we may turn our attention to several of the more important developments in public health practices in Massachusetts.

In October, 1940, the first step was taken to establish the district health officer as the administrative co-ordinator or director of state health department programs in his district. Through the use of available personnel and in some instances the transfer of personnel, the health officer in the Worcester area was sufficiently equipped to carry out a complete public health program in his constituent communities. This plan of localization was extended in February, 1941, to the Greenfield area, and in the last few months, to the Springfield and Pittsfield areas. We are, at present, completing plans to handle the work in the southern area through an office in New Bedford. The remaining districts, those in and around the Metropolitan area and on the North Shore, will be organized as soon as practicable.

This so-called "district plan" provides office space and clerical assistance for the district health officer and various field personnel, such as public health nurses, nutritionists, and sanitary officers, medical social workers and others who have hitherto worked as individuals out of either the Boston office or their own homes. Such personnel is regarded as making up the staff of the district health officer, who is responsible for the administrative direction of their field work. Each district health officer will make every effort to apprise himself of the health needs and resources of the various communities in his district and will endeavor, through the efficient use of his staff, to find a solution for these needs.

We know that this change will tend to lend dignity and responsibility to the position of district health officer and will result in a reduction of duplication of effort on the part of the state personnel. It is particularly pleasing to me, and I am sure it should be to you, to realize that the state public health program is to be supervised in each district by the district health officer, a physician and fellow member of this society.

The district plan created a need for someone in the central office whose duty it would be to effect its success. Accordingly, the position, "assistant to the commissioner," was established and charged with the responsibility of local health administration. One of his tasks is to make certain that the district health officers and their staffs

function as desired and work as well co-ordinated field units. He must maintain close contact with the division directors, be familiar with their programs and make certain that they are completely and satisfactorily carried out by the district health officers and their staffs.

With the rapid growth and development of the public health nursing activities of the department and their extension into channels other than maternal and child health, it has long been deemed more practical to administer this program from the Division of Administration rather than from a specialized division of child hygiene. Consequently, the public health nurses have been transferred from each of the divisions concerned to the Division of Administration, where they are in a unit under the direction of a chief supervisor of public health nursing. Similarly, the supervisor of medical social service was transferred from the Division of Adult Hygiene to the Division of Administration.

Responsibility for the work of these units has been delegated to the assistant to the commissioner as part of local health administration. All the changes described are in line with public health practices in the majority of the other states and in accordance with the best administrative advice on the matter.

Another new activity is a study of ragweed eradication, which has assumed an ever increasing prominence as a public health problem, since it has been estimated that between 3 and 5 per cent of the general population is hypersensitive to wind-borne pollen. Because of its many public health aspects, the Legislature directed the department to make a study concerning the eradication and control of ragweed. Observations made under this study have disclosed that, in New England, ragweed is the only important factor in late summer and fall hay fever. In addition, the discoveries that during the late summer and early fall, pollen is encountered in the air in fairly even concentrations up to the height of one mile and that it is carried by the wind for many miles have revealed that, to be of any value, control programs require the active participation of neighboring communities throughout extensive areas. Small scale campaigns are absolutely futile. With the aid of all interested official and voluntary organizations, the study is being continued to obtain as complete information as possible. Data thus compiled will become the basis of recommendations to the Legislature for ragweed elimination.

Thus far, I have said very little regarding legislation. However, it should be of interest that on a national level a very high percentage of the pending bills concern health. I should like to sug-

gest that your committee on legislative matters be thoroughly alert to the trend, particularly on the federal level, to the introduction of legislation having to do with public health. Locally, during the last several years, the Legislature has seen fit to inaugurate new health laws and amend old ones. Inasmuch as it is impossible at this time to describe all the new laws that relate to public health, I shall outline briefly one or two of the more significant ones.

Up to January, 1942, there was no law that required the licensing of hospitals; hence, the supervision of general hospitals had never been allocated to any specific state agency. There were no standards concerning their construction or maintenance, except for local fire ordinances and zoning laws. It is quite obvious that such a system was open to many abuses. Although the state laws required that clinics and dispensaries be licensed by the Department of Public Health, maternity hospitals or wards by the Department of Public Welfare, and mental-disease hospitals by the Department of Mental Health, hospitals in general were not regulated. All this was quite illogical and was not conducive to the best interests of the public. If a license is necessary for one type of hospital, it is reasonable to expect that all hospitals should be licensed. The Legislature of 1941 remedied this situation by enacting a law that made it mandatory that general hospitals be licensed by the Massachusetts Department of Public Health. An advisory committee was appointed to assist the department in formulating the rules and regulations that are being established in connection with this work. Every effort and consideration will be made not to insist on unreasonable demands on hospital administrators.

The premarital health-examination law, with its amendments, became effective on November 1, 1941. Applicants for marriage licenses must present a health certificate signed by a physician practicing in Massachusetts or by a medical officer on active service with the armed forces of the United States. Certain aspects of the law are not entirely clear at the present time, but it is expected that future amendments to clarify them will be recommended by the department at the next session of the Legislature.

The immediate objective of the Department of Public Health is to stimulate and maintain vital health services, and I take this opportunity to assure you that, as a department, we are making every effort to concentrate on services that must be kept at a maximum level during the present emergency. To avoid duplication of effort in our defense work, all such activities are being organized in the Division of Administration. Every

effort is being made to save in the use of automobiles, and we have put a number of them into dead storage for use at a future time. We realize that there will be a tendency, for economical reasons and because of pressure of other business, to cut down on accepted public-health practices in many of the communities. We are striving to prevent this. Massachusetts enjoys an enviable record in communicable-disease control, environmental sanitation, nutrition, cancer control, and medical and surgical care. Our standards must not be lowered.

The district health officers have been appointed regional directors for health by the Massachusetts Committee on Public Safety, and so far as possible, their activities have been co-ordinated. Plans are being kept up to date for the immediate mobilization of the state health personnel in any part of the State, should this necessity arise.

The department is co-operating with the Army and Navy in an effort to control syphilis and gonorrhea in the armed forces and among civilians by providing an epidemiologic service whereby nurses connected with the department directly interview infected persons for the purpose of discovering the sources of infection and the places at which contacts or exposures occurred. The information acquired by this epidemiologic investigation is utilized by the armed forces, the Department of Public Health, police agencies and other interested groups in a co-operative effort to control genitoinfectious diseases.

My foregoing remarks have been confined principally to present or past work of the department. It may be well to mention briefly what our future programs may possibly include.

As you know, the department has participated in a study of a selected number of cases of arthritis at the Massachusetts General Hospital, and it is likely that an expansion of this type of activity will result in our making a similar study, in co-operation with recognized treating agencies, of cardiac conditions, which continue to be a major cause of death in the older age groups. For some time, we have been considering, and have submitted to this society, plans for a rheumatic-fever program, which would indeed be a worth-while activity. That the department may plan for increased facilities for custodial and palliative care of cancer patients, while they await admission to and after their discharge from the Pondville or Westfield hospitals, is also logical. The Kenny method for prevention and treatment of paralysis in anterior poliomyelitis might be the subject of detailed study and evaluation as part of our crippled-children's program.

Before concluding, I wish to state that, here in

Massachusetts, we have been very fortunate in being accorded the complete co-operation of the medical profession. I emphasize the facts that without this complete co-operation our enviable record in public health would have been impossible and that a satisfactory program for the future would be in serious doubt. Be assured, that, as public-health activities expand under the stimulation of

federal agencies, we shall keep in mind the physicians' interests and, through our district health officers, shall endeavor to keep you informed of changes as they are contemplated.

I sincerely hope that these few remarks will give you a better appreciation of our administrative organization, of some of our present activities, and of a few of our possible future channels of activity.

INDUSTRIAL HEALTH AND THE WAR*

DANIEL L. LYNCH, M.D.†

BOSTON

OUR country has a war to win. President Roosevelt has said that it will be won by industrial production, that is, by the production of overpowering numbers of planes, tanks and guns and all manner of weapons and ammunition, and of fighting ships and of freighters, to bring all these arms safely and abundantly across the seas that our allies and our gallant men around the world may victoriously finish the jobs they are about. It is apparent, therefore, that our sailors and soldiers on the firing lines and our "soldiers" in overalls on the production lines are entirely dependent on each other. If production fails, our army is without weapons; if our armed forces fail, the workers in industry will become workers in chains.

Thus, the worker in industry, not only in essential war industry, but in practically all industries,—because today nearly all are contributing something to the war effort,—has been given a place of special prominence in the war. His ability to measure up to it depends heavily on his physical fitness, his freedom from preventable disease and injury, his mental stamina and his morale. Thus, loss of working time, especially by skilled workers, no matter what the cause, must be regarded today as equivalent to casualties. It is therefore our patriotic duty as physicians to contribute our best efforts to the conservation of the health of these necessary men and women in industry, so that the loss of precious work hours may be minimized.

Probably, few persons, especially persons not in industry, fully realize the demand that this war has put on the industrial manpower of the country: to build up the armed forces and to produce all the material that the armed forces will need to win the war. And probably, few persons appreciate the magnitude of the losses of manpower

from industry incurred through accidents and, especially, nonoccupational sickness.

If plans progress as scheduled for this year, the Army will be increased to 3,600,000 men, and the Navy and the Marine Corps to 1,000,000 men, a total of 4,600,000 men, virtually all of whom will have been drawn from the main industrial force. Eventually, the Army may be increased to 8,000,000 or more men. And they are the men best qualified physically and mentally for industry. They have formed the framework of all industrial production.

In peacetime, 34,000,000 out of America's labor force of 52,000,000 persons are employed in industry. Of these, about 9,000,000 have already been shifted to direct war-production activities. Watchmakers have become blacksmiths, and dungarees have replaced white collars. The number must be increased this year to approximately 18,000,000 persons to meet the production schedules laid down by the President. War this year will be the business of more than 22,000,000 of our fellow citizens. It will mean that half of all the men in the country between the ages of twenty and sixty-five years will be in the armed forces or in war production before the end of the year. It will mean the continued shifting of industrial workers from peacetime pursuits to war production, to jobs with which they are unfamiliar and with hazards to their health and safety. It will mean the absorption into war industry of several million women now engaged in home duties or unemployed whose health deserves protection. It will mean the employment in industry of the somewhat reckless young men and women between seventeen and nineteen years of age,—major accident risks,—of men past sixty years of age and of many physically handicapped persons—girls without fingers or with immobile hands and fingers, one-eyed persons and the like. It will mean that industries not directly engaged in war production, but nevertheless essential to the war effort, such as agriculture and the public serv-

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†Medical director, New England Telephone and Telegraph Company.

ices, and industries essential to the preservation of civilian morale will absorb the less physically able to work of America's labor force. It will mean an appreciable increase in accidents, occupational diseases and nonoccupational illnesses unless adequate protection for the health and safety of all these workers is provided.

Our country has the manpower and the womanpower to win this war, if they are kept vital. Therefore, industrial health becomes an acute problem: the world's greatest production unit must continue to emit the deep and resonant hum of machinery working at full efficiency.

When Japan sneaked into Pearl Harbor, everybody was grievously shocked by the report that 2600 young men had been killed. Few of us, however, are seriously impressed by the very much larger number of fatal and other accidental injuries daily occurring in civilian life—a most unfortunate situation in these days when every available man is needed, and when every hour counts in our industrial production for war.

The aggregate loss of manpower from industry because of accidents arising out of and in the course of employment is startling.² It is generally estimated that actual lost time owing to temporary disabilities sustained in occupational accidents in the United States averages at least 800,000 days each week,² or approximately 40,000,000 days each year. That equals the work days required to produce over three thousand bombers. Last year, 18,000 persons were killed in occupational accidents, and more than 90,000 others suffered permanent disabilities. Together, these accidents account for the loss of approximately 4,000,000 workdays each week, the workdays necessary to build eight destroyers.² But the time losses in industry caused by nonoccupational, off-duty accidents are far greater than all the losses due to occupational accidents and occupational diseases combined; in fact, they are more than twice as high.

Huge as these losses of vital man-hours sabotaged by accidents may appear to be, they account for only a small fraction of all the lost time in industry. Nonoccupational diseases, all the ills of the body and of the mind and the emotions to which the human flesh fell heir, deprived industry last year of approximately 3,000,000,000 work-productive man-hours, or nearly 400,000,000 work-days. Some of the loss is, of course, unavoidable, some of it can be salvaged through better placement of the worker and by preventive medicine and co-operation from the private physician, and some of it, unquestionably, can be saved by stimulating greater loyalty to the job in this critical hour. If we could save even a tenth of this lost

time due to sickness, the need for long hours of work and the seven-day week could be materially reduced, the vicious circle between fatigue and lost time broken, and production definitely increased.

These are the problems of industrial health—occupational accidents, occupational diseases, off-

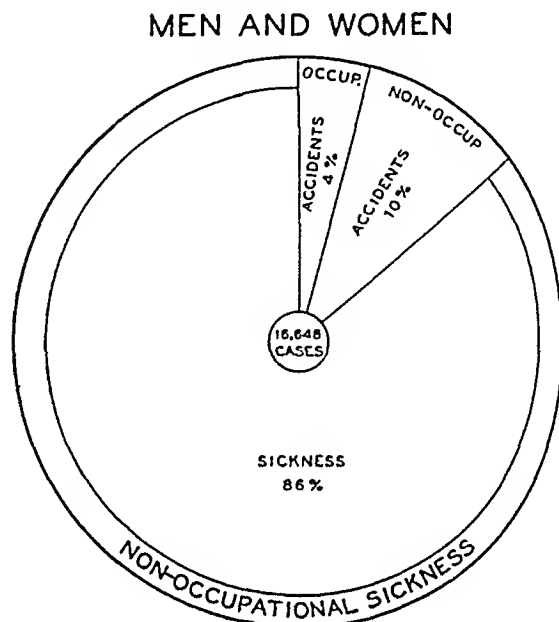


FIGURE 1. *Distribution of Lost Time (1936-1940).*

The cases include those of occupational accidents with one or more days of lost time and those of nonoccupational accidents or sickness with eight or more days of lost time.

duty accidents and nonoccupational sickness. Industrial health and industrial efficiency go hand in hand. If industrial health breaks down, production will fail. If production fails, the boys who fell at Pearl Harbor, at Bataan and at Corregidor will have made the supreme sacrifice in vain.

To maintain industrial health at a productive level is the province of industrial medicine. Industrial medicine may therefore be regarded as the science that deals with prevention, alleviation and cure of diseases that affect gainfully employed persons.³ It is a field of special medical interest comprising the practice of medical-department administration, medical supervision, preventive medicine, toxicology and public health within the confines of industry.³ Its objectives⁴ can be accomplished by the prevention of disease or injury in industry through the establishment of proper medical supervision over industrial materials, processes, environment and workers, by the health conservation of workers through physical supervision and education and by medical and surgical care to restore health and earning capacity as

promptly as possible following industrial accident or disease.

No revolutionary changes in well-managed industrial health programs for peace are required to remodel them for production for war. Health

MEN AND WOMEN

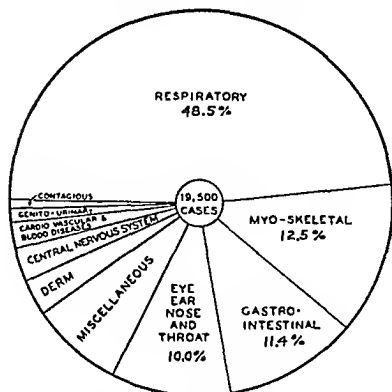


FIGURE 2. Frequency of Medical Diagnoses in Illnesses of More Than Two Days' Duration (1941).

measures that have long been recommended and used successfully in large industries should be applied with greater interest and renewed vigor and more extensively to include the small plants of 500 or less workers, where about 70 per cent of all industrial workers are employed, and where there is good reason to believe that the individual worker is exposed to more hazards or to the same hazards in more ways than the man in the large plant, because their frequency and severity rates of accident are definitely higher.

The major health measures⁴ may be enumerated as follows:

Prevention. The physician should acquaint himself, by regular inspections, with all materials and processes used in the working environment over which he has supervision, to the end that he may recommend appropriate protection of workers from conditions actually or potentially harmful.

Prevention requires provision for a safety organization with a definite and active program in accident prevention, which includes close supervision of the new inexperienced worker and the placing of the accident-prone worker in less dangerous jobs. All workers should be trained in first aid. (At the end of June, 1942, we shall

have completed the training of nearly 8000 telephone workers in five New England states in the standard first-aid course of the American Red Cross.)

Industrial physical examinations. Preplacement physical examinations should be used to fit each person to a type of work that he is able to perform continuously without undue impairment, without injury to himself or to his fellow workers and with profit to himself and to his employer. Rejections should not exceed 3 per cent.

Subsequent physical examinations should be complete enough to provide positive health protection for all workers and to safeguard public

MEN AND WOMEN

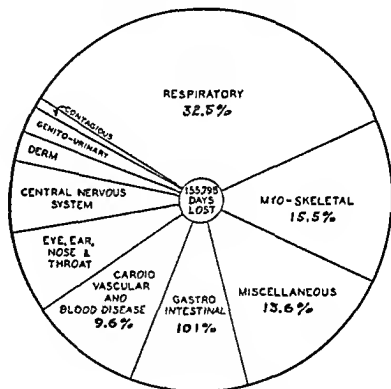


FIGURE 3. Frequency of Medical Diagnoses in Severe Illnesses of More Than Two Days' Duration (1941).

welfare. Repetition of such examinations should be governed by the circumstances of exposure and health.

Health education. The plant physician should take advantage of all opportunities for instruction of the workmen in hygienic living, both in and out of the industrial environment.

Medical and surgical care. In the treatment of compensable injuries and diseases, the disabled worker, after first-aid care, should be free to choose his physician from all those licensed doctors of medicine competent to supply the required services. The plant physician should co-operate to the end that no reasonable medical, surgical, hospital or consultative expense is spared to ensure a good end result.

The treatment of injuries or diseases not industrially induced is the function of private medical practice. In his industrial relations, the physician should abstain from such services except for minor ailments (the physician in industry may treat minor physical disorders that temporarily interfere with a worker's comfort or ability to complete a shift, and for the relief of which he may need immediate attention), first aid for urgent sickness (the physician in industry should employ such measures as the emergency dictates in all cases of urgent sickness occurring during working hours on working premises until such time as prompt notification of the family physician or family relieves him of responsibility) and rehabilitation after sickness and injury (the physician in industry can properly assume responsibility for those phases of rehabilitation after disability, industrially induced or otherwise, that progress best under controlled working conditions).

The physician in industry should be a specialist in his field. In addition to a good training and experience in the general practice of medicine and surgery and to good personal qualities, he should possess a knowledge of the detection and control of occupational diseases and be able to locate hazards and to study the earliest symptoms caused by them. He should become experienced in case

of his problems are personal as well as medical. He should know job analysis, to assist in the proper placement of new workers and in the rehabilitation and proper placement of the injured, of the worker with arrested tuberculosis and of those handicapped by heart disease, hypertension, arthritis and other chronic diseases. He should have a knowledge of factory laws and records, of compensation laws, of plant sanitation, ventilation and illumination, of accident prevention and safety and of humanitarianism. He should have had special training quite beyond the field of private practice.

War production has placed special emphasis on the factors of fatigue and nutrition for industrial workers. It is known from Britain's experience⁵ after Dunkirk that production, through the medium of the twelve-hour day, seven-day week, increased for a short time, but that accidents increased two and a half times. Within two months, production started to fall and absenteeism became general, owing in part to the fatigue or exhaustion of the workers. In 1941, a committee of the House of Commons reported that absenteeism, even during the winter, dropped about 35 per cent when the working day was reduced to eight hours.

Fatigue, in its physiologic and its psychologic aspects, is perhaps the greatest problem facing the physician in industry today. More and more, it

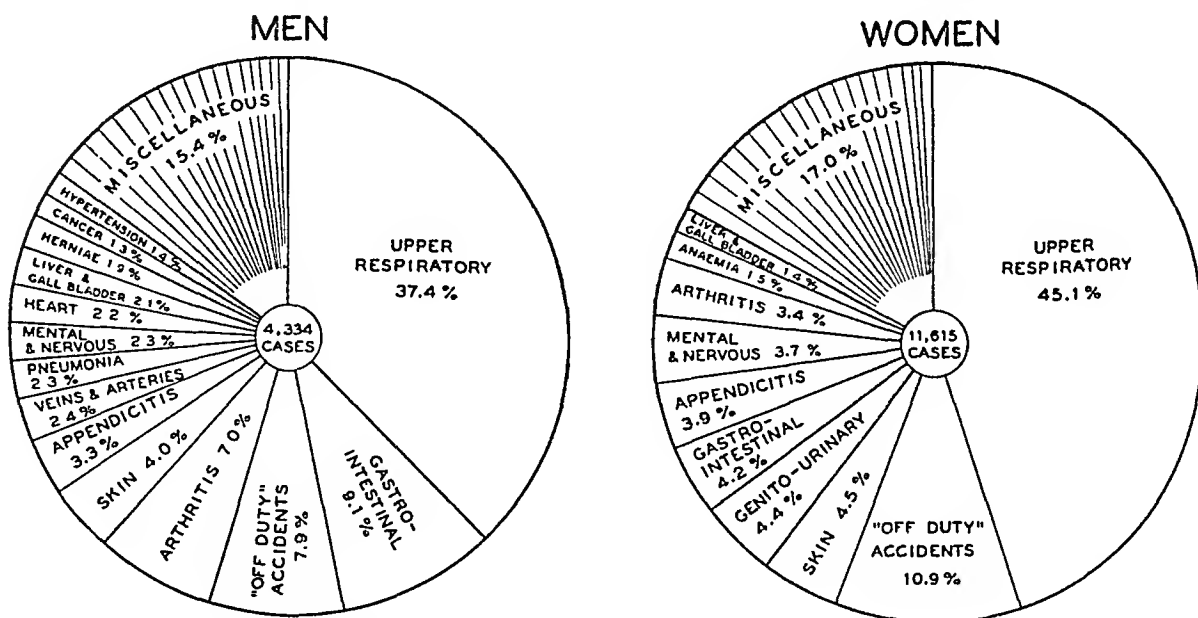


FIGURE 4. Frequency of Medical Diagnoses, According to Sex, in Illnesses of More Than Seven Days' Duration (1936-1940).

finding in communicable disease and its control. He should possess a knowledge of administration, which includes industrial relations, because many

will sabotage the output of American industry unless we profit by the experience of our allies, who had to learn the lesson by trial and error.

If all of us, particularly private practitioners, who after all, will continue to treat nearly 85 per cent of all disabilities, industrially induced or

day, the forty-hour week, the machine age, "Beauty-Rest" mattresses and other "take-it-easy" creature comforts have made "softies" out of too

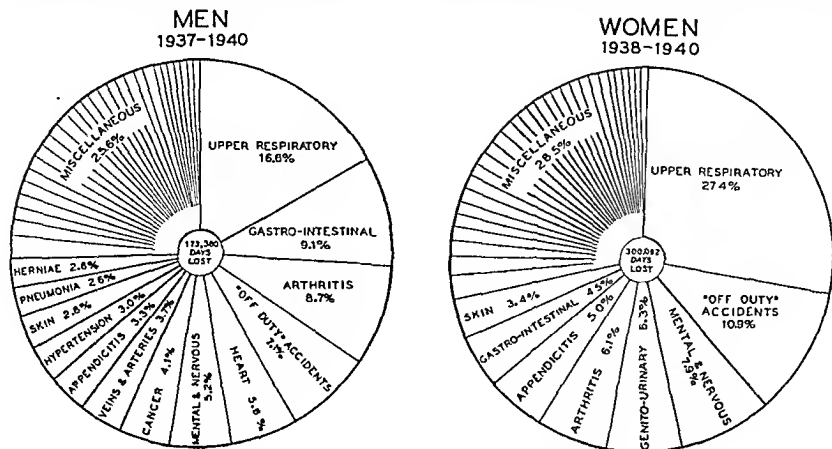


FIGURE 5. Frequency of Medical Diagnoses, According to Sex, in Severe Illnesses of More Than Seven Days' Duration.

otherwise, will give serious thought, firstly, to the great need for production to win this war and,

many of us. Perhaps, less automobiling and more footwork will make for less coronary-artery fat,

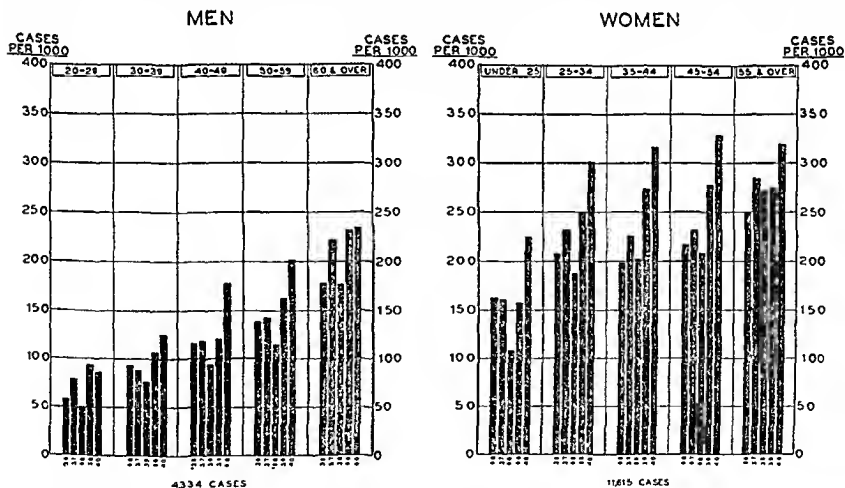


FIGURE 6. Cases of Sickness Disability, According to Age and Sex, per 1000 Workers (1936-1940).

secondly, to the reduction of industrial lost time, the need for the seven-day week and the twelve-hour day can be materially reduced. For after all, we, as a people, "can't take it" any better than our British allies: unemployment, the short work-

disability and death, and for a stronger generation to follow.

Malnutrition is a fifth columnist that erodes our war-workers from within, and works on three eight-hour shifts to produce an industrial slow-

down: insidious and unseen, it may well be an underlying cause of absenteeism, industrial accidents and lowered production. It has been clearly demonstrated that persons on deficient diets soon

There is just a little more to wartime industrial health, as suggested by Dr. Elton Mayo, of the Harvard Business School. Industry must abandon the philosophy of "take care of the technical situa-

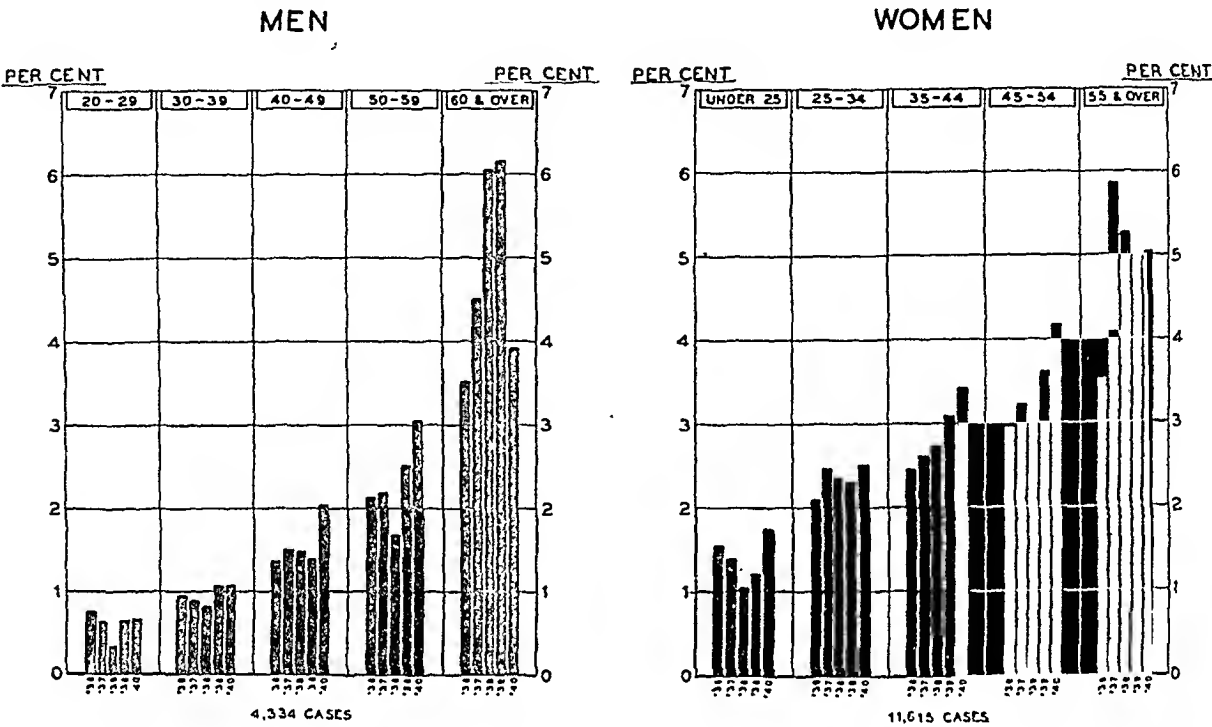


FIGURE 7. Percentage of Total Calendar Days Lost Owing to Sickness Disability, According to Age and Sex (1936-1940).

develop fatigue, mental depression, general weakness and loss of morale. Inadequate facilities for

tion and let humanity handle itself." It must realize "that sentiment is perhaps more important

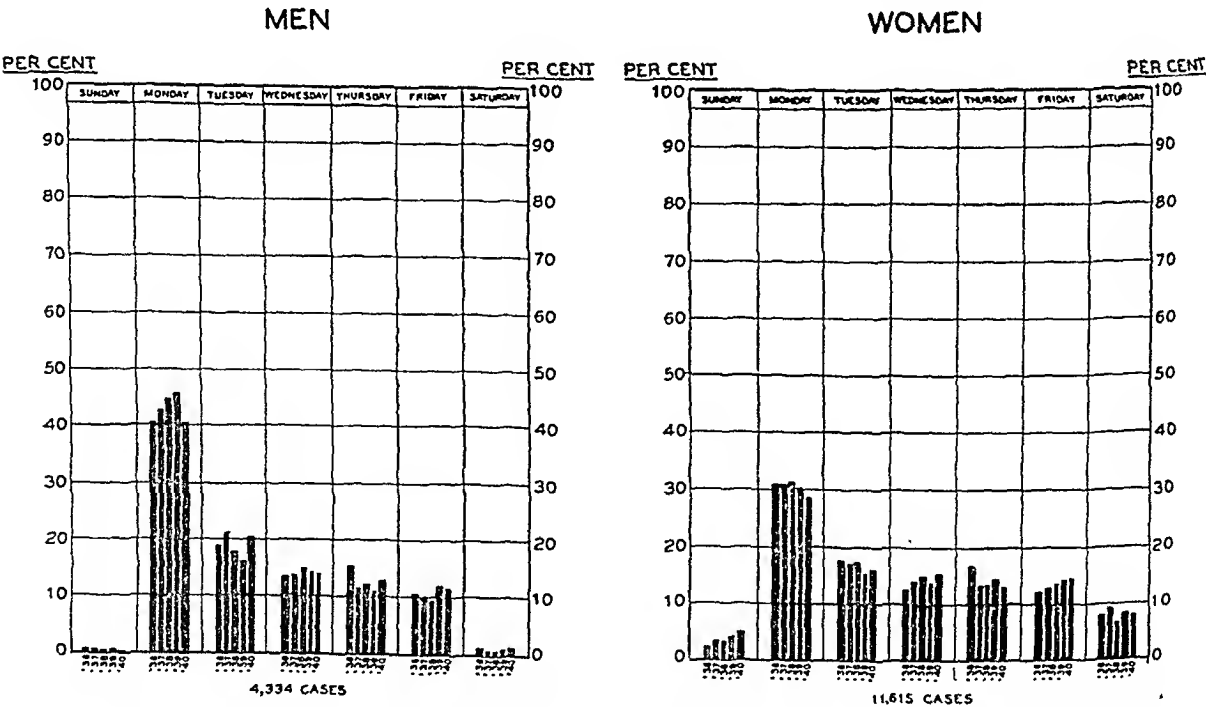


FIGURE 8. Distribution of Cases of Sickness Disability by the Day Absence Began, According to Sex (1936-1940).

lunch and insufficient time for eating are, at the present time, justifiable causes for dissatisfaction among workers in many plants and on all shifts.

than logic in dealing with workers; that the men at the bench have feelings other than those expressed in terms of hours and wages, that they need social

not so great, but there is pictured the upward trend of disability frequency as women advance in age. This increase was consistent from year to year, and it emphasizes the problem of industrial health as it is affected by the older employees.

Figure 7 demonstrates the severity of illness with increasing age; although men under thirty lost only about 0.7 per cent of available work time because of illness, men over 60 lost nearly 5 per cent. The situation was similar among women, the length of their absences increasing with age, regardless of its cause.

Figure 8 is interesting. It shows the frequency with which absences began on the several days of the week. One wonders why such a large proportion of all disabilities began on Monday. It may be that workers did not feel quite up to par at the end of the week, but remained on to finish out the week; or it may mean that a good many of them had a "bad week end."

More interesting, however, is Figure 9, which indicates the day of return to work following disability, regardless of the day on which disability began.

Among men, nearly 70 per cent returned to work on Monday, and the same thing was true for nearly 60 per cent of the women. Production must continue on other days of the week, as well as on Monday, and those concerned with production cannot understand why workers who have recovered from illnesses wait until Monday to return to work. To a large extent, it is a psychologic problem—the thought of beginning the week right. Unquestionably, the private physician can help a great deal in this respect: a great deal of lost time can be regained if he will permit and encourage his patients to return to work as soon as they are able.

245 State Street

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ROBERT BURTON AND HIS DRUGS: THE ARMAMENTARIUM OF 1600*

CLIFFORD S. LEONARD, PH.D.†

BURLINGTON, VERMONT

IN THE second partition of Robert Burton's *Anatomy of Melancholy*, which appeared in London in 1621 and in which the author dealt with the cure of melancholy, one finds a discussion "of Physick which cureth with medicines, and of medicines purging melancholy and of those curing head melancholy and hypochondriacal or windy melancholy."

Burton was not a physician, but he was a learned man who had read the works of those before him and of his contemporaries, and had sifted out the gist of their recommendations. At that time, the doctrine of the four humors and the temperaments prevailed, and there was no science of anatomy or of physiology for physicians. Vesalius had begun to influence surgery, but internal medicine remained medieval.

Burton began by railing at physic a bit:

The country people use kitchen physick and common experience tells us they live freest from all manner of infirmities that make least use of apothecaries physick. . . . Some think the physicians kill as many as they save and who can tell how many murders they

make a year, *quibus impune licet hominum occidere*, that may freely kill folk and have a reward for it? And, according to the Dutch proverb, a new Physician must have a new Church-yard, and who daily observeth it not?

However, after further such diatribe, he hastened to say: "But I will urge these cavelling and contumelious arguments no farther, lest some physician should mistake me and deny me Physick when I am sick; for my part, I am well persuaded of Physick."

Burton proceeded to single out some of the chief and best recommended drugs of the pharmacopeias and herbals at his disposal. He divided all simple medicines into alteratives and purgatives. It is his list of simples that is considered here. He had comparatively little use for compound formulas or for powdered precious stones, although he devoted a small space to them. The purgative simples were divided into those purging upward (emetics) and those purging downward (cathartics). He also divided the simples as having particular virtues for particular parts of the body:

As to the head, Aniseeds, Foalfoot, Betony, Calamint, Eyebright, Lavender, Bays, Roses, Rue, Sage, Marjorum, Peony, etc.; for the lungs, Calamint, Liquorice, Enula

*From the Department of Physiological Chemistry and Pharmacology, University of Vermont College of Medicine.

†Assistant professor of pharmacology, University of Vermont College of Medicine.

Campana, Hyssop, Horehound, Water Germander, etc., for the heart, Borage, Bugloss, Saffron, Balm, Basil, Rosemary, Violet, Roses, etc.; for the stomach, Wormwood, Mints, Betony, Balm, Centaury, Sorel, Purslain; for the liver, Dartsphine, Germander, Agrimony, Fennel, Endive, Succory, Liverwort, Barberries; for the spleen, Maidenhair, Finger-fern, Dodder of Thyme, Hop, the rind of Ash, Betony; for the Kidneys, Grumel, Parsley, Savitfrage, Plantain, Mallow; for the womb, Mugwort, Pennyroyal, Fetherfew, Savine, etc.; for the joints, Camomile, St. John's Wort, Organ, Rue, Cow slips, Centaury the less, etc.

How many of Burton's drugs have persisted through the ages? How many were official in the pharmacopoeia and formularies as late as the turn of the twentieth century? I have made a list, finding for Burton's old common names the

Latin names of his galenicals, and then determined whether they were in the *U. S. Pharmacopoeia VII* (1894) and whether they are still in the *U. S. Pharmacopoeia XI* (1936) or in the *National Formulary V* (1926) or *VI* (1936). I also consulted certain editions (1914, 1926 and 1932) of the *British Pharmacopoeia*. Furthermore, by referring to the 1894 edition of the *U. S. Dispensatory*, as well as the 1938 edition, I ascertained whether the drugs that were not in the official and semiofficial lists chanced to be mentioned in Part II of these dispensatories. The citation of Burton's drugs in Table 1 may not be complete, but the one hundred and thirty-eight items given suffice to demonstrate how Burton's drugs have withstood the centuries.

TABLE 1. *Burton's Drugs and Their Survival to Modern Times.*

LATIN NAME	BURTON'S NAME	MODERN NAME (IF DIFFERENT)	BURTON'S THERAPEUTICS	MODERN THERAPEUTICS
<i>Scorvus colamus</i>	Colamus aromatics	Sweet flag	For flatulence	USP 1894, NF 1936 aromatic, for flatulence
<i>Adiantum capillus veneris</i>	Maidenhair		For the spleen	Disp 1938 pectoral
<i>Agrimonia eupatorium</i>	Agrimony		For the liver	Disp 1938 astringent, tonic
<i>Ajuga chamaepitys</i>	Dartsphine	Ground pine	Diuretic, for the liver	Disp 1938 diuretic
<i>Aloe Perryi</i>	Vloes	Secotrine aloe	Purge	USP 1936 cathartic
<i>Ambergris</i>	Ambergris		For flatulence	Disp 1938 antispasmodic
<i>Ammi cithraga</i>	Ammi	Bishop's weed	For flatulence	Disp 1938 stomachic
<i>Ammonium chloridum</i>	Ammoniac	Ammonium chloride	Mild purge	USP 1936 saline; expectorant
<i>Amomum melegueta</i>	Grana paradisi		For flatulence	Disp 1938 stomachic, spice
<i>Anacyclus pyrethrum</i>	Pellitory		Mucatoric	USP 1894 rubefacient, analgesic
<i>Anchusa officinalis</i>	Bugloss		For melancholy, for the heart	Disp 1938 stomachic, diuretic
<i>Anethum graveolens</i>	Dill		Diuretic	B P 1926 diuretic
<i>Angelica archangelica</i>	Angelica		For flatulence	Disp 1938 stomachic
<i>Anthemis nobilis</i>	Camomile		For the joints, for flatulence	USP 1894, BP 1926 stomachic
<i>Antimonium sulfidum</i>	Antimony	Antimony sulfide	Emetic	BP 1926 emetic
<i>Aristolochia rotunda</i>	Aristolochy	Somewort	For flatulence	Disp 1938 tonic
<i>Artemisia abrotanum</i>	Southernwood		For baths	Disp 1938 mentioned
<i>Artemisia al synthium</i>	Wormwood	Absinthe	For the stomach	Disp 1938 stomachic
<i>Artemisia vulgaris</i>	Mugwort		For melancholy, for the uterus for the spleen	Disp 1938 ebolic
<i>Arum maculatum</i>	Dragon's root	Cuckoo's pint	Mild purge	Disp 1938 expectorant
<i>Asarum ceterach</i>	Asarabacca, foet's foot	Asarum	Emetic, for the head, diuretic	Disp 1938 emetic, errhine
<i>Asplenium ceterach</i>	Ceterach, finger fern		For the spleen	Disp 1938 urther <i>Asplenium</i> mentioned, probably antihelmintic
<i>Atropa mandragora</i>	Mandrake		For sleep	Disp 1938 depressant (atropine and mandragora)
<i>Berberis vulgaris</i>	Barberry		For the liver	BP 1914, NF 1936 astringent, cathartic
<i>Betonica officinalis</i>	Beinny		For the head, for the stomach, for the spleen	Disp 1938 aromatic; astringent
<i>Borago officinalis</i>	Borage		For the head, for the heart	Disp 1938 demulcent
<i>Brassica nigra</i>	Mustard		For flatulence	USP 1936 condiment, emetic
<i>Coffea arabica</i>	Coffee		For the head	NF 1926 stimulant, flavor.
<i>Calendula officinalis</i>	Marigold		For melancholy	USP 1894, NF 1936 antispasmodic
<i>Cannabis sativa</i>	Hemp, hving	India hemp	For sleep	BP 1926, NF 1936 hypnotic
<i>Carum carvi</i>	Cary	Caraway	For flatulence	USP 1936 stomachic
<i>Caryophyllus aromaticus</i>	Clove		For flatulence	USP 1936 carminative
<i>Cassia fistulosa</i>	Cassia		Purge	USP 1894, BP 1932, NF 1926 purgative
<i>Cassia senna</i>	Senna		Purge	USP 1936 purgative
<i>Castor</i>	Castor	Glands of beaver	For melancholy, errhine	Disp 1938 antispasmodic
<i>Chicorium endivia</i>	Endive		For the stomach	Disp 1938 mentioned
<i>Chicorium intybus</i>	Chicory succary		For melancholy	Disp 1938 reputed tonic, in jaundice
<i>Cnicus benedictus</i>	Carduus benedictus	Thistle	Emetic	Disp 1938 emetic
<i>Colchicum autumnale</i>	Hemodictylis	Colchicum	Purge	USP 1936 in gout, palliative
<i>Colutea arborescens</i>	Colutea	Bladder senna	Mild purge	Disp 1938 purgative
<i>Combretaceae Terminalis</i> (5 species)	Mylrabalan		Purge	Disp 1894 astringent, cathartic
<i>Convolvulus scammonium</i>	Scammony		Purge (by suppository)	Disp 1938 purge (Mexican scammony, an <i>Ipomoea</i> , in NF 1936)

TABLE 1 (Continued)

LATIN NAME	BURTON'S NAME	MODERN NAME (IF DIFFERENT)	BURTON'S THERAPEUTICS	MODERN THERAPEUTICS
<i>Crocus sativa</i>	Saffron		Soporific, for the heart	USP 1894, NF 1936 coloring matter
<i>Curcuma zedoaria</i>	Zedoary		For flatulence	NF 1926 aromatic, for flatulence
<i>Cuscuta epithymum</i>	Epithyme dodder of thyme		For the spleen	
<i>Cuscuta europaea</i>	Dodder		Mild purge	
<i>Cyclamen hederacifolium</i>	Cyclamen	Sow bread	For flatulence, purge	Disp 1938 purgative
<i>Datura stramonium</i>	Datura stramonium	Thorn apple jimson weed	For melancholy	USP 1936 nerve depressant
<i>Daucus carota</i>	Daucus	Carrot seed	Diuretic	Disp 1938 diuretic
<i>Dictamnus albus</i>	Dictamn		Purge of melancholy	Disp 1894 sedative in hysteria
<i>Drosera ros solis</i>	Ros solis	Sundew	For melancholy	Disp 1938 other <i>Drosera</i> cited as inert
<i>Electuarium lentum</i>	Confection of senna		Lentive purge	USP 1894 BP 1932 mild purgative
<i>Elettaria repens</i>	Carduans	Cardamom	For melancholy, for flatulence	USP 1936 aromatic, carminative flavor
<i>Euca sativa</i>	Rocket		Aphrodisiac	
<i>Erythraea centaureum</i>	Centaur		Mild purge	Disp 1938 tonic, laxative
<i>Euphorbia lathyris</i>	Caper	Caper spurge	Purge	Disp 1938 diuretic, oil, a cathartic
<i>Euphrasia officinalis</i>	Eyebright		For the head	Disp 1938 reputed for toothache, eyes and catarrh
<i>Foeniculum vulgare</i>	Fennel		For the liver, diuretic	USP 1894, NF 1938 (oil), USP 1936 aromatic carminative
<i>Fraxinus excelsior</i>	Rind of ash	Ash bark	For the spleen	USP 1894 for rheumatism and gout
<i>Fraxinus ornus</i>	Manna		Purge	USP 1894, NF 1936 gentle laxative
<i>Fumaria officinalis</i>	Fumitory		Purge	Disp 1938 tonic laxative
<i>Genista tinctoria</i>	Genist	Broom dyer's broom	For flatulence	Disp 1938 purgative
<i>Globularia alpinum</i>	Alpinus	Wild senn of Europe	Purge for flatulence	Disp 1938 mild purgative
<i>Glycyrrhiza glabra</i>	Liquorice		For the lungs	USP 1936 flavor, demulcent
<i>Gurcumeum</i>	Gurcume		For melancholy	NF 1936 nauseant, purgative
<i>Helleborus niger</i>	Black hellebore		Drastic purge	Disp 1938 emetic cathartic cardiac
<i>Hepatica triloba</i>	Liverwort	Hepatica	For the liver	Disp 1894 tonic astringent demulcent
<i>Humulus lupulus</i>	Lupulus	Hops	For the spleen for the blood for melancholy	USP 1890 NF 1936 tonic, bitters
<i>Hypericum perforatum</i>	St John's wort		For melancholy, for the joints	Disp 1938 reputed in hysteria and mania
<i>Hyssopus officinalis</i>	Hyssop		For the lungs for flatulence	Disp 1938 carminative expectorant
<i>Inula helenium</i>	Enula campana	Elecampane	For flatulence	USP 1894 expectorant
<i>Juniperus sabina</i>	Juniper berries, sabine		For the uterus, for flatulence	USP 1936 (oil) carminative diuretic
<i>Ipomoea turpenthum</i>	Turbeth	Turpenth	Purge	BP 1932 purge (jalap group)
<i>Lactuca sativa</i>	Lettuce		Sedative	Disp 1938 inert
<i>Lapis Armenum</i>	Armenian stone		Simple purge	Disp 1894 Armenian bole mentioned as an antacid
<i>Lapis lazuli</i>	Lapis lazuli		Purge	Lazurite contains sodium sulfide and aluminum silicate
<i>Laurus nobilis</i>	Laurel or bay	European laurel	Emetic	Disp 1938 spice, stomachic
<i>Latendula vera</i>	Lavender		For the head	USP 1936 (oil) aromatic stimulant flavor
<i>Laterdula stoechas</i>	Stoechas		Mild purge of melancholy	Disp 1894 tonic stomachic
<i>Lithospermum officinale</i>	Gromel	Gromwell	For the kidneys	Disp 1938 reputed diuretic
<i>Malva sylvestris</i>	Mallows		For the kidneys	Disp 1938 demulcent, sometimes used in kidney disease
<i>Maranta galanga</i>	Galanga or China root		For flatulence	Disp 1938 stimulant, aromatic
<i>Marrubium vulgare</i>	Horehound		For the lungs	USP 1894 tonic, laxative for cough
<i>Melissa officinalis</i>	Balm		For the head, for the heart	USP 1894 diaphoretic, antispasmodic
<i>Mentha pulegium</i>	Pennyroyal		For the uterus for flatulence	Disp 1938 stomachic, abortifacient
<i>Mercurialis annua</i>	Mercury herb		Purge	Disp 1938 diuretic
<i>Myristica fragrans</i>	Nutmeg		Soporific, for flatulence	USP 1936 aromatic, flavor, sedative ec-bolic
<i>Nicotiana tabacum</i>	Tobacco		Emetic	USP 1894 emetic
<i>Nymphaea odorata</i>	Water lily		Soporific, anaphrodisiac	Disp 1938 reputed anaphrodisiac
<i>Ocimum basilicum</i>	Ocyme or basil		For the heart	Disp 1938 aromatic, condiment demulcent
<i>Origanum vulgare</i>	Origan or marjoram		For the joints for flatulence for the head	Disp 1938 tonic, condiment stomachic
<i>Paeonia officinalis</i>	Peony		For melancholy, for the head	USP 1894 antispasmodic, in epilepsy
<i>Papaver somniferum</i>	Poppy	Opium	Soporific	USP 1936 narcotic
<i>Petroselinum hortense</i>	Parsley		For the kidneys	USP 1894 ec-bolic, antipyretic
<i>Pimenta officinalis</i>	Allspice		For flatulence	USP 1894 NF 1936 carminative
<i>Pimpinella anisum</i>	Anise seed		For flatulence, diuretic	NF 1936 (oil) carminative flavor
<i>Piper nigrum</i>	Pepper		Errhine	USP 1894, NF 1936 carminative sternu-tory
<i>Plantago major</i>	Plantain	Plantain	For the kidneys	Disp 1938 diuretic (Psyllium seed NF 1938 purgative)
<i>Polypodium vulgare</i>	Polypody	Polypody fern rock brake	Purge	Disp 1938 pectoral, demulcent, purgative, antihelmintic?
<i>Polyporus officinalis</i>	Agaric	Agaric mushroom	Purge	Disp 1894 anciently reputed in consumption
<i>Portulacca oleracea</i>	Purslain		For melancholy	Disp 1938 diuretic?

TABLE I (Concluded)

LATIN NAME	BURTON'S NAME	MODERN NAME (IF DIFFERENT)	BURTON'S THERAPEUTICS	MODERN THERAPEUTICS
<i>Primula officinalis</i>	Primrose cowslip			Disp 1938 mentioned
<i>Pyrethrum (Chrysanthemum) parthenium</i>	Feverfew, feverfew		For the uterus	Disp 1938 action like camomile
<i>Rheum officinalis</i>	Rhi bath		Purge	USP 1936 purgative
<i>Rosa centifolia</i>	Rose		For the head	USP 1894 NF 1936 (<i>Rosa gallica</i>) as stringent tonic
<i>Rosmarinus officinalis</i>	Rosemary		For flatulence	USP 1936 (oil) aromatic stimulant
<i>Rumex acetosa</i>	Sortel	Dock	For the stomach	Disp 1938 astringent diuretic
<i>Ruta graveolens</i>	Rue		For flatulence	Disp 1938 astringent diuretic
<i>Salix alba</i>	Willow		For sleep	Disp 1936 contains salicin
<i>Salvia officinalis</i>	Sage		For flatulence for the head	NF 1936 astringent aromatic flavor
<i>Santalum album</i>	Sandels	Sandalwood	For flatulence	USP 1894 NF 1936 expectorant aromatic
<i>Sassafras sarisfolium</i>	Sassafras	Sassafras	For flatulence	USP 1936 (oil) aromatic carminative flavor
<i>Satureja hortensis</i>	Calimint		For the head for the lungs	Disp 1938 mentioned
<i>Satyrion</i>	Satyrion	An orchid	For the head	
<i>Saxifrage cordifolia</i>	Saxifrage		For the kidneys	Disp 1938 a little
<i>Scolopendrium vulgare</i>	Scolopendrite		For the spleen	Disp 1894 astringent demulcent
<i>Scorzonera hispanica</i>	Black salsify		For melancholy	
<i>Smilax china</i>	China	China root	For melancholy	Disp 1938 diuretic
<i>Smilax officinalis</i>	Sarsaparilla		For melancholy	USP 1936 diuretic, for syphilis
<i>Solid nitras</i>	Saltpeter	Sodium nitrate	Purge	USP 1926 saline cathartic diuretic
<i>Solanum dulcamara</i>	Solanum	Nightshade	For sleep	NF 1936 sedative
<i>Sonchus oleraceus</i>	Sow thistle		For the blood	Disp 1938 cathartic
<i>Tamarix gallica</i>	Tamarisk	Larch	For the spleen	BP 1914 astringent, expectorant
<i>Taraxacum officinale</i>	Dandelion		For the blood for melancholy	USP 1894 NF 1936 bitter, stomachic
<i>Terebinthina</i>	Cyprian turpentine	Turpentine	For flatulence	NF 1936 not recommended internally
<i>Teucreum chamardrys</i>	Germannder		For the lungs	Disp 1938 colorant
<i>Teucreum scordium</i>	Scordium	Water germander	For the lungs	Disp 1938 colorant
<i>Thymus vulgaris</i>	Thyme		Preparative	NF 1936 (oil) pectoral
<i>Urginea maritima</i>	Scilla sea onion	Squills	Emetic	USP 1936 emetic cardiac
<i>Urtica dioica</i>	Nettle seed		For flatulence	Disp 1938 diuretic
<i>Valeriana jatamansi</i>	Spiknard (oil)		For flatulence	Disp 1894 expectorant
<i>Valeriana officinalis</i>	Valerian		For flatulence	USP 1936 sedative of smooth muscle
<i>Valeriana album</i>	White hellebore		Emetic cathartic	Disp 1938 emetic cardiac (V. viride in USP 1936)
<i>Verbasum thapsus</i>	Verbascum	Mullen		NF 1926 demulcent
<i>Vitex agnus castus</i>	Agnus castus		For flatulence	King's 1m Disp 1898 anaphrodisiac
<i>Viola odorata</i>	Violet		For the heart	Disp 1938 demulcent laxative emetic
<i>Zingiber officinalis</i>	Ginger		For flatulence	USP 1936 aromatic spice

One concludes from the above list that, of the one hundred and thirty-eight drugs, fifty-eight were still official or semi-official in 1890, whereas fifty of these have persisted to the present decade. Of the rest, all but about six are described as drugs in a modern source, the *Dispensatory*.

Burton lived just before the influx of drugs from the Americas, when such important items as quinine and ipecac arrived—long before Withering and his digitalis, and longer still before Claude Bernard and the beginning of experimental medicine. But, for Burton's day, this was a sane list, amid many semimagical offerings. True, he mentions one author who praises the virtue of taking one hundred and one eggs, three at a time, but with the knowledge of vitamins today, eggs in such large "doses" might have some therapeutic effect. He mentions the virtue, at seasonable times, of being seasick.

It seems remarkable that there existed therapeutic nihilism, too, before his time, for Burton quotes an author (Girolamo Cardano, 1501-1576) who could "cure all diseases with water alone."

Does that not sound like the present school whose dictum is "rest and forced fluids"?

No wonder Burton spurned compound formulas, the "dia-this" and "dia-that," the confections, the electuaries, the theriaca (treacles) and the mithridates. The following is the formula* of the

R	Gm. vel cc
Trochique of squills	360
Trochique of the bodies of vipers	180
Hedysaron	
Long peppers	
Tincture of opium	33 160
Red roses	
Dried glycyrrhiza	
Turnip seed	
Water germander	
Balm of Gilead	
Cinnamon	
Agaric	22 90
Costus root	
Indian card	
Dicamum of Crete	
Rhapontic	
Cinquefoil root	
Ginger	
White marubium	
Arabic storach	
Flowers of fragrant jonquils	
Macedonian parsley seed	

*This is taken from the second edition of a French work, *Pharmacopoeia Royale Galienique et Chymique* (Lyon 1753), by M. de Charas and is one of the traditional formulas for this medicament. The first edition of Charas's work was issued in Paris in 1746 and thus may have been seen by Burton. The formula made 40 pounds but the pharmacist doubtless did not set about making up this item too often.

Mountain calamin		
Aromatic coffee		
Saffron		
Black and white pepper		
Triglodite myrrh		
Frankincense		
Chian turpentine	āā	45
Gentian root		
True acorus		
Spignel		
Great valerian		
Celtic nard		
Cardamoms		
Ground pine		
St. John's wort		
Ammi seed		
Thalaspia seed		
Anise seed		
Fennel seed		
Hartwort of Marseilles		
Little cardamoms		
Malabathrum		
Tufts of <i>Polii montani</i>		
Germander		
Carpobalsam		
Juice of hypocists		
True acacia		
Gum arabic		
Calamite storax		
Lemnian earth		
Chalcite		
Sagapenum	āā	30
Little aristolochia root		
Little centaury points		
Cretian wild carrot seed		
Opopanax		
Galbanum		
Judean pitch		
Castor	āā	15
Good honey		12,684
Good wine	q.s.	

Make a treacle according to the art.

Sig: Take one teaspoonful at bedtime, followed by a glass of wine. Two teaspoonfuls may be taken if necessary.

"Theriaca of the Elder Andromanchus," originally in Latin, which has been translated into English and the metric system.

The indications were paralysis, apoplexy, epilepsy,

lethargy, convulsions, diarrhea and dysentery, as a vermifuge, as an antidote to poisons, for malaria and pest smallpox, against the bites of mad dogs and snakes, for insomnia, for hysteria, for icterus and for "infinite other maladies." Each 75 gr. was stated to contain 1 gr. of opium. Hence, a teaspoonful would give about 0.06 gm. opium, or a full adult dose.

One did not in those days compound such a treacle in the amount of a single prescription. One can think of the assistants pounding mortars for days before the assembly of the mixture.

Accordingly, Burton did not hold theriacas in repute, and it can be seen why. He preached moderation. And, strangely enough, in therapeutics, he found authority for this in the writings of Arnold of Villanova, who lived from 1235-1312. Burton quotes Arnold as follows:

And this no other which I say than that which Arnoldus prescribes in his 8 Aphoris: *A discreet and godly Physician doth first endeavor to expel a disease by medicinal diet, then by pure medicine*, and in his 9th: *he that may be cured by diet must not meddle with Physick*. So in Aphoris 11: *A modest and wise Physician will never hasten to use medicines, but upon urgent necessity, and that sparingly too*.

Can those who today teach pharmacology and therapeutics think of a better tag for the end of their course of lectures, a better *envoi* to the students, than these words of Arnold's from the year 1300?

MEDICAL PROGRESS

NUTRITION: THE APPEARANCE OF THE TONGUE AS AN INDEX OF NUTRITIONAL DEFICIENCY*

HAROLD JEGHERS, M.D.†

BOSTON

THE old-time practitioner paid considerable attention to the appearance of the patient's tongue; much helpful information was undoubtedly secured. It is the purpose of this review to point out that the modern physician can use this simple clinical observation to a much better advantage than his predecessor.

In his recent monograph, Thoma¹ states, "The tongue is probably a better indicator of somatic disturbances than any other part of the oral mucosa." The literature of the last ten years indicates this to be especially true for the various nutritional deficiency disorders. To clarify this aspect of the subject, it is necessary to review briefly the anatomy of the tongue and the lingual manifestations of systemic disorders, as well as primary lingual diseases that may be confused with the manifestations produced by the nutritional deficiencies.

Diagnostic Importance of Tongue In General Practice

Changes in the tongue are numerous and reflect, or are actually diagnostic of, many systemic disorders other than nutritional deficiencies. Means,² Comroe³ and Kennedy⁴ have briefly discussed some of these. The monographs by Prinz and Greenbaum⁵ and Thoma⁶ do so in greater detail and include many colored plates of representative lesions. A study of these plates is helpful, since the color of lingual lesions is often of prime value in diagnosis and yet very difficult to visualize from a written description. The tongue reflects the degree of jaundice, pallor or cyanosis, at times of pigmentation and more rarely of purpura. Changes in taste or in movement and the onset of paralysis or tremors are of value in neurologic diagnosis. The tongue is enlarged in cretinism, myxedema, monoglossism, acromegaly, angioneurotic edema, infectious glossitis and so forth. Rarely, one may see the Lubarsch-Pick syndrome (systematized amyloidosis with macroglossia).⁷ The Liebermeister syndrome is diagnostic of air embolism.⁸ A num-

ber of dermatologic conditions have associated lingual lesions, as do certain of the blood dyscrasias, drug eruptions and uremia. Dameshek and Henstell⁹ have emphasized the characteristic appearance of the tongue in polycythemia vera. McCarthy,¹⁰ Comroe³ and Brown and Haffner¹¹ have discussed some of the commoner disorders localized in or peculiar to the tongue. These include leukoplakia, cancer, chancre, tertiary syphilis, lingual thyroid, benign tumors, traumatic ulcers, glossitis rhomboidea mediana and so forth. These conditions, even though numerous and varied, are usually distinctive in appearance and can be readily differentiated from the lingual changes due to nutritional deficiencies. The latter are discussed in detail elsewhere in this paper.

Simple inspection with the naked eye or with an ordinary magnifying glass (2 or 3x) gives all the information required. Trueblood¹² advises that the tongue be palpated with the gloved fingers. This procedure, by evaluating the degree of induration, is helpful in diagnosing cancer, chancre and so forth, but is not required to detect the changes caused by the deficiency states. Glossitis and other lingual changes should be differentiated from buccal mucositis,[‡] gingivitis and cheilitis.

Anatomy of Tongue

The ability of the tongue to reflect so many systemic changes is inherent in the unique histologic structure of the dorsum of the tongue anterior to the V-shaped groove, the sulcus terminalis of His, which separates the anterior from the posterior portion or root. The undersurface of the tongue is covered by thin, smooth mucous membrane identical in structure, appearance and color with the rest of the buccal mucosa. The mucous membrane of the posterior dorsum of the tongue is thick, freely movable and of clinical interest only because of the numerous lymphoid follicles (lingual tonsil) present there.¹⁴

*The term, "stomatitis," is commonly used in the literature to include involvement of the mucous membrane of the tongue, buccal mucosa, mucosa of the palate, gums and lips in a process resulting from irritation, infection or deficiency. The epithelium of the buccal mucosa, palate and undersurface of the tongue is different from that of the dorsum of the tongue. One may be involved without the other and certainly may differ in its response to the same exciting pathologic agent. Since there is no suitable term (comparable to glossitis for the dorsum of the tongue) to signify involvement of the mucous membrane of the buccal mucosa, palate and undersurface of the tongue, Weisberger¹³ suggests buccal mucositis as an appropriate term. Gingivitis (for the gums) and cheilitis (for the lips) are, of course, well understood.

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*From the Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals, the Fifth and Sixth (Boston University) Medical Services, Boston City Hospital, and the Department of Medicine, Boston University School of Medicine.

†Assistant professor of medicine, Boston University School of Medicine physician, clinical staff, Evans Memorial, Massachusetts Memorial Hospitals, junior visiting physician, Boston City Hospital.

The anterior dorsal covering of the tongue is adherent to the muscular tissue and consists of a corium or mucosa rich in vessels, nerves and lymphatics covered by stratified squamous epithelium, similar to but thinner than the skin, arranged for the most part as numerous papillae. There are eight to twelve large, round, circumvallate papillae arranged in a V just anterior to the sulcus terminalis. Most of the anterior dorsum is covered with numerous filiform papillae, thin, barblike squamous epithelial projections. They hide the underlying vascular mucosa and, being relatively opaque squamous cells (similar in a lesser capacity to those that make the skin appear white), give the tongue its normal whitish-pink color in contrast to the red color of the lips and buccal mucosa. There is a continual regeneration and shedding of the squamous epithelium of these papillae similar to the squamous cells of the skin.

The fungiform papillae appear as rounded bright-red eminences among the whitish-pink filiform barbs, larger but much fewer and sparser on the dorsum than at the tip and edge of the tongue. The fungiform papillae appear red because the capillary-containing mucosal portion is covered by only a thin layer of epithelium in contrast to the thicker epithelial layer of the filiform papillae. The epithelium of the filiform papillae appears sensitive to many metabolic changes; it may proliferate more rapidly, making each papilla appear whiter and thicker, or desquamate more readily, exposing the underlying mucosa. The latter condition gives the tongue a smooth red appearance and renders the red fungiform papillae more prominent. The epithelium of the fungiform papillae is more resistant to such changes. The circumvallate papillae are affected least of all.

Dry Tongue

Means² has stressed the fact that dryness of the tongue is "the best clinical index of the state of hydration of the body," especially if oliguria, with urine of high specific gravity, is a concomitant finding. The simplicity of lingual inspection makes this a most valuable bedside observation. Mouth breathing, although likely to dry the surface, does not give the tongue the dry, shriveled appearance of a true dehydration. Gregersen and Bullock's¹⁵ demonstration of a close correlation between the volume of the plasma and the flow of saliva appears to give scientific support to the above clinical axiom. Kirk,¹⁶ on the other hand, was unable to correlate the plasma chloride concentration or the degree of dehydration with the condition of the tongue. He believes that dryness of the tongue is better correlated with the degree of intestinal motor paralysis.

The problem is further complicated by the repeated observation that dryness of the tongue often accompanies glossitis, especially that due to deficiency of nicotinic acid¹⁷ and probably from other factors of the vitamin B complex as well. The tongue becomes moist again following appropriate vitamin therapy. Invariably, such persons have atrophic glossitis. Although the mechanism is not clear, it appears that one may expect to see dryness of the tongue in deficient vitamin states as well as in dehydration. Nicotinic acid has been reported as a successful remedy for xerostomia—a condition characterized by chronic dry mouth.¹⁸

Coated Tongue

The coated tongue has probably occasioned more concern in the layman's mind than in medical circles. Interpreted in the light of modern knowledge, the coat on the tongue may have diagnostic and prognostic significance with relation to the deficiency disorders. Essentially, the coat on a tongue consists of increase and thickening of the desquamating squamous epithelium of the filiform papillae, in addition to mucin, food debris, mouth organisms and leukocytic exudate caught on or between the filiform barbs. The color is white, but may be changed by tobacco, coffee, food or medicinal substances and so forth, since the desquamating epithelium is more readily stained than other cells. A slight coat on the tongue is a common normal finding, especially on the less mobile posterior portion. Failure of the self-cleansing mechanism of normal mastication and salivation causes it to increase. Indeed, a unilateral coating may be noted when half the tongue is immobilized by paralysis.⁴ When dehydration is severe, the coating may become dried and matted together, giving the *encrusted tongue*.

Rhoads¹⁹ believes that, in some cases at least, the old-fashioned coated or furred tongue represents beginning necrosis of the filiform papillae. As the condition progresses, the coating becomes more marked until finally the epithelium of the papillae desquamates, leaving the typical slick, red atrophic surface of a vitamin B complex deficiency glossitis. It is a well-confirmed observation that a coated tongue is rarely seen in any of the forms of atrophic glossitis. When therapy is given, the papillae grow in again. The return of a normal surface makes a coating again possible. In other words, the integrity of the papillae is necessary for a coat on the tongue. An increase in the coating may indicate an early deficiency state, and a smooth tongue, with the absence of any coating, an advanced deficiency condition.

A noticeable coat on the tongue is common in many infectious diseases, probably most notably in

scarlet fever. Within forty-eight hours in this disease, the engorged and enlarged red fungiform papillae protrude above a thick white lingual coat caused by hypertrophy and increased desquamation of the filiform papillae to give the characteristic *strawberry tongue*. Then follows desquamation of the white filiform barbs, revealing a smooth, somewhat granular purplish-red lingual mucosa—the typical *raspberry tongue*. The resemblance of this raspberry tongue to the magenta glossitis of ariboflavinosis has aroused comment, but proof of this etiology is lacking. Within a week or more, the papillae of the scarlet-fever tongue regenerate, with return of the normal lingual appearance.

One may speculate on the possibility that infectious diseases influence the lingual papillae by interfering with proper metabolism of the various factors of the vitamin B complex. The lingual coat in scarlet fever may be more striking than in other infectious diseases because the enanthem operates in addition to the mechanism just mentioned. Resolution of this problem may prove to be a fruitful bit of research.

Oatway and Middleton²⁰ found a correlation of coated tongue with the degree of gastric acidity. Of 55 patients with coated tongues, 11 had achlorhydria, 2 hypochlorhydria, 17 hyperchlorhydria, and 25 normal acidity.

Pellagrous Glossitis

Spies and Cooper,²¹ in their review of the clinical features of pellagra, stress the frequency and severity of glossitis and include a colored plate of the most typical lesions. Others give similar descriptions.^{22, 23} Early, there is swelling and redness of the tip and lateral margins of the tongue, and the papillae may be engorged; atrophy of the papillae may follow later, but is not prominent early. The reddening assumes a fiery-scarlet hue. Ulcerations may form, and often become covered with a greyish membrane in which Vincent's organisms may be found. Swelling, tenderness, pain and salivation may be prominent.¹⁷ If the condition persists, the papillae may atrophy, and the tongue may become dry.¹⁷ The dramatic response to niacin (nicotinic acid) therapy—with blanching of the redness within twenty-four hours and the healing of atrophic or ulcerative areas, and even disappearance of the associated Vincent's infection, in forty-eight to seventy-two hours—leaves no doubt about the specificity of this type of glossitis.

A somewhat similar type of glossitis, but not accompanied by the other usual clinical features of pellagra, has been frequently reported, often in epidemic proportions, in such varied places as Palestine,²⁴ China,¹⁷ India^{25, 26} during the siege of Madrid²⁷ and elsewhere.²⁸ The glossitis in these

epidemics usually, but not always, responded to niacin therapy. These so-called "epidemics" occurred when large numbers of people were fed insufficient amounts of the same kind of food. This type of glossitis was in a sense considered "larval" pellagra.

Field, Parnall and Robinson²⁹ stress the fact that in the Northern part of this country pellagra is often atypical in appearance and different from the full-blown classic syndrome seen in the South. Lesser changes than a red, sore, atrophic tongue may be present. Sometimes, the tongue is merely swollen, somewhat painful and showing indentations from the teeth. At times, the lingual changes are those seen in the nondescript atrophic glossitis, which is described in a later section. The non-lingual aspects of this atypical pellagra syndrome are described in detail. This concept of pellagra is of special interest to the practitioners of New England.

Riboflavin-Deficiency Glossitis

The distinctive features that characterize the lingual changes attributable to riboflavin deficiency were first described by Jolliffe, Fein and Rosenblum³⁰ and Kruse, Sydenstricker, Sebrell and Cleckley.³¹ In contrast to the fiery-red color of pellagra, the tongue in ariboflavinosis is magenta or purplish red. The epithelium over the papillae does not desquamate, but appears flattened and edematous, with resultant "mushroom-shaped" papillae that give the surface of the tongue a finely "pebbled" or granular appearance. Hence, the synonyms—pebbled tongue, granular tongue and magenta tongue—applied to this form of glossitis. Fissures may develop. The tongue may be painful, may have a burning sensation, and may even cause some dysphagia on swallowing. These lingual changes may precede and almost constantly accompany the cheilosis and seborrheic dermatitis of this deficiency state. Features of riboflavin deficiency helpful to diagnosis have been reviewed elsewhere.³² Sydenstricker et al.³³ noted frequently that the red and atrophic tongue of pellagrins treated with niacin, with diets low in riboflavin, changed, over a period of weeks, to a magenta glossitis that, in turn, cleared up when riboflavin therapy was instituted. Weisberger,³⁴ on the other hand, believes that the glossitis of riboflavin deficiency is characterized by a primary lingual coating followed by a patchy oval desquamation, with the center atrophic and the edges whitish pink and raised. He believes that the specificity of these changes rests on their improvement with riboflavin therapy. However, this is not the generally accepted point of view.

The cause of the magenta color in the riboflavin-deficient tongue is not clear. Sydenstricker et al.³³

studied the dorsum of these tongues in living patients with a microscope (magnification, 20x) and described the flattened papillae as "looking more like a dead jelly fish that has been washed up on the beach than anything else, a round translucent hemisphere with the capillaries lying deeply in a loose coil."

A logical explanation for this color change appears as follows: capillary dilatation and proliferation are prominent features in ariboflavinosis and undoubtedly take place in the mucosal portion of the papillae. If the capillaries are dilated, one may postulate that the circulation of red corpuscles through them may be slowed. The overlying epithelium is not desquamated but thinned and perhaps edematous. These dilated capillaries, with their stagnant blood flow seen through the changed epithelium, give the resultant magenta color to the tongue. The rapid blanching of the tongue following riboflavin therapy further supports this explanation. The normal tongue, in contrast, has a pinkish-white color because the underlying capillary loops of the mucosal portion of the papillae are covered by a partially opaque stratified squamous epithelium. The tongue in niacin deficiency and in the commoner atrophic glossitis, on the other hand, is scarlet or beefy red, because the overlying epithelial cells of the papillae desquamate, causing the capillary loops in the mucosal base of the papillae to be more prominent and their color more apparent. In addition, there seems to be a capillary response similar to inflammation in niacin deficiency.

Glossitis From Other Deficiencies

Lingual changes due to deficiencies other than niacin or riboflavin undoubtedly occur, but are, as yet, not well delineated. There appears to be no oral lesion characteristic of thiamine deficiency. Glossitis did not develop in human subjects placed on a thiamine-deficient diet.³⁵ There is the suspicion that vitamin A deficiency may produce hyperkeratotic changes in the oral mucosa.

Rosenblum and Jolliffe²³ noted cases of glossitis that failed to respond to niacin or riboflavin but improved with the use of vitamin B₆ (pyridoxine). They believe there may be lingual changes characteristic of pyridoxine deficiency. These tongues are described as smooth, slightly edematous, occasionally painful and of a peculiar purplish hue. Unfortunately, the full acceptance of this important observation is conditioned by the suggestion of others that pyridoxine may be necessary at times for the utilization of riboflavin.³³ Deficiency of other less well-known fractions of the vitamin B complex may cause lingual changes. This possibility is suggested by the response of glossitis to yeast or liver extract after failure to respond to

the well-known pure vitamins such as riboflavin and niacin.³⁶ The cause of glossitis in pernicious anemia is not entirely certain.

Waldenström and Hallen's³⁷ studies indicate that iron deficiency may cause lingual changes that revert to normal with the use of iron alone. Glossitis is frequently present in the idiopathic hypochromic anemia of women,³ an iron-deficiency disorder.

There is some evidence that the use of the estrogens either increases the demand for or suppresses the utilization of the vitamin B complex. Ashworth and Sutton³⁸ reported that the administration of estrogens to persons with a subclinical vitamin B complex deficiency produced glossitis as well as other lesions characteristic of a complete deficiency in the vitamin B complex.

Hunter's Glossitis

Hunter,³⁹ in 1909, studied the glossitis of pernicious anemia, attributing it to an infectious process. As late as 1927, Schneider and Carey⁴⁰ presented evidence to support this. Although the tongue in pernicious anemia may become infected secondarily, there seems but little doubt that the glossitis is on a deficiency basis. Lewis,⁴¹ in 1930, summarized the evidence for this. It is a clinical characteristic of pernicious anemia that the glossitis accompanies relapses and clears with control of the anemia.

The subjective complaints of pain, burning and numbness are often a prominent feature, even at a time when gross changes are minimal, being especially prominent when spicy, salty or hot foods are placed in the mouth. Occasionally, small vesicles are noted about the edges that may break down and form tiny ulcers. The description of atrophic glossitis to follow later applies as well to Hunter's glossitis. A striking feature in severe relapses of pernicious anemia may be the contrast of the red atrophic tongue against the pallor of the buccal mucosa.

According to Castle,⁴² the cause of glossitis in pernicious anemia is not entirely certain but, as suggested by the high incidence of achlorhydria in this disease, is conditioned by the absence of the so-called "gastric intrinsic factor." Thus, the glossitis of patients with pernicious anemia does not respond to experimental therapy with beef muscle unless normal human gastric juice is given simultaneously. In certain cases of sprue, however, the glossitis may improve with beef muscle alone, presumably because of the natural presence of gastric intrinsic factor.⁴³ Ventriculin and liver extract, which are effective remedies for the sore tongue in these conditions, so act because they contain a product of the interaction between a

food factor and gastric intrinsic factor derived from the normal animal. Castle⁴² does not believe that the glossitis in pernicious anemia has any features that separate it from other forms of glossitis. Manson-Bahr⁴⁴ goes even farther: he believes that a glossitis of similar nature and nonspecific to the disease is found not only in pernicious anemia but also in sprue, pellagra, nutritional anemias and idiopathic steatorrhea.

Restoration of the tongue to normal, with regeneration of papillae, commonly follows the remission of pernicious anemia with liver extract therapy. This process has been followed objectively with the use of tongue prints.²⁰

Myxedema (especially when anemia is prominent) and pernicious anemia are often confused with each other and may actually coexist. Means⁴⁵ points out that a red atrophic tongue is common in myxedema and increases the difficulty of this differential diagnosis. The person with myxedema is likelier to have a large clumsy tongue, pain being a less prominent feature, in contrast to the smaller but more painful tongue in pernicious anemia.

The term Hunter's glossitis may appropriately be applied to the lingual changes of pernicious anemia, but it implies no distinctive features of specific diagnostic value. The complaint of a sore tongue and the finding of glossitis suggest the diagnostic possibility of, but do not prove, the presence of pernicious anemia. All the diseases mentioned in the section on atrophic glossitis must be considered in the differential diagnosis.

Moeller's Glossitis

Moeller's glossitis, also known as glossitis marginalis exfoliativa or chronic superficial excoriations of the tongue, appears to be a poorly defined lingual condition that may be related to some deficiency state. Prinz and Greenbaum⁵ consider it synonymous with Hunter's glossitis of pernicious anemia. Thoma,⁶ on the other hand, believes it to be of varying etiology, and includes allergy, drug eruptions and neural disturbances as possible causative factors in addition to nutritional deficiency.

It consists of irregular, but well-defined atrophic areas, which are limited most frequently to the sides and tip of the tongue, are bright red, are never coated and are persistently painful. In fact, pain appears to be one of the most prominent features and is made worse by acid or hot foods, spices and so forth. It may be confused with "wandering rash" of the tongue. From the nutritional point of view, Moeller's glossitis appears to be a painful form of atrophic glossitis, the areas of atrophy being limited in extent and most fre-

quently localized to the lateral edge and tip of the tongue. Its characteristics appear too indefinite for one to consider it a distinct entity.

Atrophic Glossitis

An atrophic glossitis not readily recognizable as due to any specific vitamin deficiency appears to be a common clinical finding. It is variously called atrophic glossitis, bald tongue, slick tongue, bald tongue of Sandwith, beet-red tongue and beefy-red tongue. Rhoads¹⁹ expressed his inability to predict which therapy would be effective from the appearance of the tongue. Since in clinical practice deficiencies are multiple, it is to be expected that most cases of glossitis will be of complex origin and not one of the clear-cut specific lingual syndromes previously described.

This type of glossitis^{2-4, 6, 20, 46-48} begins with desquamation of the epithelium of the filiform papillae at the tip and sides of the tongue. At times, small vesicles form and break down. The affected area appears red (atrophic), and may be painful if the desquamation is deep enough. Later, the filiform papillae over the dorsum desquamate. The tongue then appears red and smooth, with the fungiform papillae still prominent. Even the latter may eventually flatten and disappear. At this stage, the tongue has the appearance of a piece of raw red meat. The papillae are said to regenerate in the reverse order with appropriate therapy. These tongues may be dry, and at times some loss of taste is experienced. Because the circumvallate papillae seem to escape gross changes, the gustatory sense is not noticeably altered. If the tongue is slightly swollen, impressions from the hard palate and teeth may be noted on the dorsum or edges. Frequent comment can be found concerning the absence of a coat on the atrophic tongue.

Usually, the nature of the deficiency cannot be told from the appearance of the tongue. However, Kuo and Huang¹⁷ believe that niacin deficiency is a main, but not necessarily the sole, feature when ulcers are present and inflammatory changes (scarlet hue) with minimal papillary atrophy are prominent findings in the glossitis. Atrophy of the papillae, with but little inflammation (a smooth pinkish-red tongue), is more suggestive of a liver-extract deficiency. Patients with atrophic glossitis should be treated with the whole vitamin B complex, that is, yeast or crude liver extract, in addition to such pure vitamins (riboflavin, niacin and so forth) or iron as seem indicated by the clinical evidence for their deficiency. Disappearance of the glossitis with regeneration of papillae has been noted in from five to thirty days in many patients thus treated.

Glossitis of this type has been noted in^{3,4} pernicious anemia, sprue, achlorhydric hypochromic anemia, pellagra, Plummer-Vinson syndrome, chronic dysentery, jejunostomy, intestinal stricture, dibotriocephalus-latus infestation, achlorhydria, steatorrhea⁴⁴ and myxedema.⁴⁵ Manson-Bahr⁴⁴ has reviewed this subject at great length. The high incidence of achlorhydria in almost all these conditions has been frequently commented on.^{3,4}

Oatway and Middleton,²⁰ in a detailed study, correlated the lingual changes with the gastric acidity, using tongue prints, made on smoked paper that was shellacked, to secure objective detail. Their work indicates that papillary atrophy was rare when normal acidity or hyperacidity was present, and frequent with achlorhydria. This study gives support to the clinical impression that achlorhydria and atrophic glossitis are frequently associated. Hutter, Middleton and Steenbock⁴⁸ produced smoothing of the highly serrated papillae of the tongues of rats kept on a diet deficient in vitamin B complex. Elsom⁴⁹ noted soreness and glossitis in a human subject placed on a diet deficient in the vitamin B complex. This did not clear with thiamine but responded to other factors in the B complex. This fact and the frequent response of glossitis to the various forms of therapy mentioned strongly support the contention that the presence of glossitis is a most valuable clinical sign and indicative that some form of nutritional deficiency is present.

Many workers believe that that appearance of the tongue may mirror the appearance of other portions of the gastrointestinal mucosa. The aphorism, "raw red tongue, raw red gut,"⁴¹ has some objective proof to support it. Spies, Bean and Ashe⁵⁰ reported that pellagrins who were gastroscopied had a mucous membrane of the stomach similar in appearance to the stomatitis in the oral cavity. A patient studied at the Evans Memorial Hospital by Ingelfinger⁵¹ is especially illuminating in this regard. This man, in his late thirties, had an ileostomy of long standing, performed because of intestinal obstruction of benign nature. He developed vitamin B complex deficiency, with a glossitis similar to the type mentioned above. The mucosa of the ileum, which could be readily inspected at the site of the ileostomy, was bright red and smooth and appeared edematous. Following appropriate vitamin therapy, both the glossitis and the injection of the ileum improved; the mucosa of the ileum became pink, and its pattern more prominent. Manson-Bahr⁴⁴ found by sigmoidoscopy that the rectal mucosa was hyperemic in acute sprue associated with glossitis and resembled in a general sense the changes seen on the tongue.

Wandering Rash of Tongue

Wandering rash of the tongue appears to be the accepted term for the not uncommon condition known also as geographic tongue, erythema migrans, exfoliativa areata linguae and numerous other synonyms.^{5,6,52} It begins as a faint grey or whitish patch anywhere on the anterior dorsum of the tongue. The epithelium of the filiform papillae over this area desquamates, exposing the smoother red surface of the underlying mucosal layer, the isolated fungiform papillae appearing as shiny, red eminences. Thickened filiform papillae form a whitish border about these atrophic red areas, which are usually oval or circular in outline. These atrophic spots migrate continually but irregularly, the epithelium desquamating at one point and regenerating at another, to form bizarre circinate or geographic patterns. The spots may migrate within hours, days or weeks, may remain fixed for days or years, or may clear completely or return repeatedly at varying intervals for many years. Since only the superficial epithelial layer is involved, symptoms are usually absent, and the patient may not be aware of its presence. Greenbaum⁵³ has described a painful form, which appears to be rare.

Wandering rash of the tongue may be readily confused with the atrophic glossitis of deficiency disease. Yet it appears etiologically unrelated to any of the vitamin deficiencies. The patchy desquamation described by Weisberger¹³ for riboflavin deficiency is histologically different. Rhoads⁵⁴ has not seen a cure of this condition from the use of vitamin B complex therapy. When the atrophic patches are along the lateral aspects of the tongue, it may be readily confused with Moeller's atrophic glossitis, but the frequent presence of pain in the latter condition serves to make their differentiation possible.

Wandering rash is common in children, but may be seen at all ages and may appear periodically or continuously throughout life, with perhaps a tendency to disappear as middle age is reached. Prinz and Greenbaum⁵ consider it a local expression of a constitutional neuropathic anomaly. Thoma⁶ believes that there is some evidence for a hereditary background. No therapy is required in most cases.

Grooved Tongue

Grooved tongue, also known as fissured, furrowed or scrotal tongue, a congenital anomaly present in about 0.5 per cent of the tongues of the human race irrespective of age, is commoner in men and often inherited through the male sex.⁵ The monograph by Prinz and Greenbaum⁵ contains a detailed description of this condition and

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**CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL**ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor***CASE 28321****PRESENTATION OF CASE**

A fifty-seven-year-old widow was referred to the hospital by her physician because of an upper abdominal mass.

Seven weeks prior to admission, when the patient was examined by her physician because of an upper respiratory infection, a mass was felt in the upper abdomen. When specifically questioned, she recalled vague abdominal discomfort unrelated to her dietary habits. Her appetite had always been good. No bowel habit changes were recalled except for diarrhea on a single day two weeks prior to admission. The stools had been normal in appearance.

The past history was not remarkable except for an operation on the thyroid gland performed one year previously. The menopause occurred seven years before admission. There had been no bleeding since then. During the five months prior to admission, the patient noted ankle swelling in the evening; there was no associated dyspnea or orthopnea.

Physical examination revealed a well-developed, slightly obese woman who was in no discomfort. The pharynx and tonsils were congested. There was slight spasm in the right upper abdomen, and a mass could be felt in this region. The heart and lungs were normal, and the rest of the physical examination was negative.

The temperature was 98.6°F., and the pulse 100. The blood pressure was 120 systolic, 74 diastolic.

The blood was normal. The urine was normal except for 10 to 15 white blood cells per high-power field and a slight growth of *Staphylococcus albus*. The stool was brown and guaiac negative.

A barium enema revealed several diverticula of the descending colon. A gastrointestinal series and intravenous pyelogram were negative. A Graham test showed no concentration of the dye in the gall bladder. No stones were demonstrated. The abdominal flat film showed a round soft-tissue shadow about 11 cm. in diameter in the right midabdominal field overlying the crest of the ilium and lower pole of the right kidney. Review of these films showed that the soft-tissue

mass was inferior to the liver and produced little pressure on the colon.

On the twelfth day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT R. LINTON: In summary, this fifty-seven-year-old woman apparently had a mass in the right upper quadrant, with very few if any related symptoms. What are the possibilities with a mass in the right upper abdomen? One thinks first of gall-bladder conditions. A second possibility is a tumor of the right portion or hepatic flexure of the colon. A third is a tumor involving the right kidney. Other remote possibilities are gumma of the liver, tumor of the pancreas and echinococcal cyst. Certainly, we have no evidence that the last was present, and we have no laboratory findings to help us out on that diagnosis. Tumor of the head of the pancreas of that size would certainly have produced some signs of biliary obstruction, which were not present. A tumor involving the lower pole of the kidney is apparently ruled out because of the negative pyelogram. The question of hepatic-flexure growth can also be fairly well ruled out, I believe, by the barium enema, which was negative except for the diverticulosis, which I do not believe played any part in this patient's story. The hepatic flexure is known to be hard to visualize by x-ray, but I think we can rely on the report that the barium enema was negative for a lesion in this portion of the colon. In addition, there was a negative guaiac test on the stool.

The question of gall-bladder disease should be seriously considered. I do not believe it is necessary for patients with gall-bladder disease to have many gastrointestinal symptoms. Certainly, this patient had a minimum, if one accepts the story as it is written here.

One other condition that might be considered is a fibroid of the uterus. It is unusual to see fibroids above the pelvis, especially in the right abdomen, but I know that they do occur there. An ovarian cyst should also be thought of. I think these are unlikely, however, in view of the fact that the patient was seven years past the menopause. Before going on any farther with the discussion, I think we might see the x-ray films.

DR. LAURENCE L. ROBBINS: The mass is rather hard to see on these films, but this is its location. It apparently causes a little pressure on the proximal portion of the transverse colon. The mass appears to be homogeneous, and is of soft-tissue density.

DR. LINTON: Should you say that it was above the transverse colon?

DR. ROBBINS: I should say that it was. I think this represents the mass here.

A PHYSICIAN: Is there a kidney film?

DR. ROBBINS: There is a film in which one can see the right kidney, which seems to be all right. The film was taken to show the gall bladder; it shows the right-kidney shadow very clearly, however.

DR. LINTON: The intravenous pyelogram does not show any abnormality?

DR. ROBBINS: It does not show any pressure on the calyces that I can see.

DR. LINTON: It also shows the kidneys very well. The mass as I see it is a rather spherical one. Is that right?

DR. ROBBINS: Yes.

DR. LINTON: It is rather unusual for a gall-bladder shadow. However, it is located in the proper position—under the inferior surface of the liver and pressing the hepatic flexure and transverse colon downward.

One other condition that I had not considered is mesenteric cyst. I do not know any way to rule it in or out, but I think it is a possibility. The mass seems too far lateral on the right side to suggest a pancreatic cyst. I think the differential diagnosis lies between a dilated gall bladder, a hydrops of the gall bladder with a stone impacted in the ampulla and a tumor of the lower pole of the kidney, without evidence of pressure on the kidney; in view of the x-ray film, I must make a diagnosis of hydrops of the gall bladder. The negative Graham test adds support to this diagnosis.

CLINICAL DIAGNOSIS

Hydrops of gall bladder.

DR. LINTON'S DIAGNOSIS

Hydrops of gall bladder, with stone impacted in ampulla.

ANATOMICAL DIAGNOSES

Hydrops of gall bladder.

Acute and chronic cholecystitis.

Cholelithiasis.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was explored, and a very large, greatly dilated gall bladder was found. When it was opened, it contained nearly colorless bile. It showed a number of small white stones. The walls showed both chronic and acute inflammation, and there was one abscess in the wall. It is a little surprising that the patient did not have some evidence of systemic reaction

because there was quite marked infection, as well as mechanical stasis.

DR. LINTON: What was the obstruction due to?

DR. MALLORY: I should have mentioned that a stone was impacted at the mouth of the cystic duct.

CASE 28322

A sixty-year-old man entered the hospital complaining of dysphagia of two weeks' duration.

The patient was well until six months before admission, when he began to feel weak and run down and noticed that he was losing weight. Approximately two months before admission, because of continued weight loss, he consulted his physician, who had a chest plate taken and told the patient that he had tuberculosis. Three weeks later, he entered another hospital; at the time, he had a slight cough productive of white sputum. No tubercle bacilli were found in the sputum on repeated examinations, and a chest plate was said to have been somewhat characteristic of tumor. Two weeks before admission, the patient had a severe paroxysm of coughing and raised about 30 cc. of bright-red blood. This was followed immediately by persistent dysphagia, which increased so that at the end of a week he was able to swallow only small amounts of ice water and subsisted on parenteral fluids. There had been no vomiting, regurgitation or other symptoms referable to the gastrointestinal tract or respiratory system. The patient was transferred to this hospital, and on admission his cough was still productive of about a cupful of white sputum each day. He had lost 60 pounds, and complained of profound weakness.

The patient's father had died at seventy-three of a tumor in the abdomen.

On examination, the patient was extremely emaciated, dehydrated and weak. Examination of the chest showed poor aeration throughout the right lung, with absent signs at the base, more prominent posteriorly, and diminished to absent breath sounds over the upper lobe. There was no apparent shift of the mediastinum, and the left lung was clear. The heart was normal. Abdominal and rectal examinations were negative.

The temperature was 99.2°F., and the pulse and respirations were normal. The blood pressure was 120 systolic, 80 diastolic.

The urine was normal. Examination of the blood showed a red-cell count of 3,500,000 with a hemoglobin of 12.7 gm. (photoelectric-cell technique), and a white-cell count of 52,000 with 93 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 16 mg. and the protein 5.1 gm. per 100 cc.; the chloride was 104.2

milliequiv. per liter, and the carbon dioxide combining power 29.9 vol. per cent. A blood Hinton reaction was negative.

X-ray films of the chest showed a large mass in the posterior upper mediastinum that displaced the esophagus and trachea forward. A large portion of this mass was seen to lie in the tracheo-bronchial angle. There was extensive mottled consolidation in the lower portion of the right lung field, which, in the lateral view, was seen to correspond mainly to the lower lobe, with possible involvement of the middle lobe. The chest was large, particularly in the precordial space, and the diaphragm was low.

On admission, attempts to pass stomach tubes of various sizes met with obstruction in the mid-esophagus. A barium swallow the following day showed extrinsic pressure on the esophagus, and a moderate amount of barium passed into the stomach. Following this procedure, the patient was able to take esophageal feedings. The esophagus was dilated with bougies, and he could swallow water and food, nourishment being supplemented by intravenous fluids. Two weeks after admission, the sputum became copious and purulent. X-ray therapy was started, but the first treatment had to be discontinued because of the patient's condition. He rapidly failed, and died on the seventeenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. HELEN S. PITTMAN: The sequence of events in this case is weakness and weight loss, cough and, finally, bleeding after a very severe paroxysm of cough. Immediately after this, the patient had dysphagia, which increased in a week to a point where he could swallow only small amounts of ice water. There had been no symptoms pointing to the gastrointestinal tract until immediately after the severe cough and hemorrhage.

Two months before admission, when the only complaints were weakness and weight loss, a chest plate showed something interpreted as tuberculous. I believe this was the "extensive mottled consolidation in the lower portion of the right lung field" that was present on our films. The film three weeks later, by which time the patient had a slight cough, was said to have been more characteristic of tumor. I interpret this as referring to the large mass visible in the mediastinum, which either did not show up on the first film (and I think it might easily have been missed on a posteroanterior film) or had increased in size in three weeks.

The severe paroxysm of cough might have been caused by pressure or by aspiration, but it would not have produced 30 cc. of blood unless the act of coughing ruptured something. The dysphagia that followed suggests that there was internal as

well as external bleeding, producing a hematoma that pressed on the esophagus.

On admission, the patient was emaciated and dehydrated. The red-cell count and the protein of 5.1 gm. per 100 cc. are consistent with his malnutrition. The other chemical levels are within the normal range. The white-cell count of 52,000 makes one think at once of leukemia. We are not given a description of the smear, but are told only that there were 93 per cent polymorphonuclears. In the absence of any information about abnormal cells, this may be interpreted as indicating suppuration. Two weeks after admission, the sputum became copious and purulent. This I interpret as drainage of multiple small pulmonary abscesses that, undrained, had been responsible for the leukocytosis. I suppose one should consider the possibility of trauma from the passage of bougies, with subsequent infection, but I shall not do so in view of the elevated white-cell count on admission.

There were apparently two lesions within the chest,—the mass in the mediastinum and the right-lower-lobe disease,—and it is of the utmost importance in arriving at a diagnosis to try to decide which came first. If we accept the sequence as demonstrated by the x-ray films and assume that the intrapulmonary disease came first, we may say that the mass represented mediastinal metastasis or abscess. I have never seen a metastasis like this, and I do not believe the patient was sick enough for this to have been a mediastinal abscess.

It seems reasonable to assume that the mass was the older, even though it was not seen on the first x-ray film. The commonest tumor of the posterior mediastinum is neurofibroma. These tumors frequently arise from the wall of the esophagus but do not invade it, therefore giving external pressure only. The simple cysts of the mediastinum that I have seen have been lower. They usually arise from bronchial epithelium and therefore lie anterior to the esophagus. However, hemorrhage in a cyst with external leak would account for the sequence of bleeding and sudden dysphagia, and must be considered. Leakage from an aneurysm might behave in the same way, but the site of this mass would correspond to the ascending aorta, which was anterior and not posterior; the blood Hinton reaction was negative; finally, although we are given no fluoroscopic note of whether or not the mass pulsed, we know that x-ray treatment was planned, and I think aneurysm, unless nonpulsating because of laminated clot so that the fluoroscopist was misled, may be excluded. Lymphoma must be included in every such differential diagnosis. I see no way to rule it in except by x-ray response. The patient

could not tolerate even one treatment, but I attribute that to his general condition, for there was not time for it to have been reaction to x-ray therapy. An intrathoracic thyroid gland lies anterior, and a dermoid cyst and sarcomas are usually anterior. Carcinoma of this size arising from a bronchus should cause bronchial obstruction and atelectasis, and there were none.

Whatever the nature of the mediastinal mass, we must not forget the process in the right lower lobe. There was poor aeration throughout the right lung, with "absent signs" at the base, whatever that means. That does not help much, for, if the lesions were central, there need have been no characteristic physical signs. Aspiration pneumonia is usually bilateral but may occur on one side, and the right lower lobe is said to be the commonest site. However, it seems unlikely that the patient could have aspirated sufficient food to give this reaction without any conscious dysphagia. We have no information to suggest phlebitis, from which he might have had pulmonary emboli. Spontaneous abscess is usually single rather than multiple.

The patient was weak and run down, and lost weight for almost five months before he had any cough. This is not too uncommon in carcinoma of the bronchus. Infection distal to bronchial carcinoma is almost the rule, although when there is sufficient obstruction to allow infection behind it, there should be a wheeze if one listens for it. Patients with bronchial carcinoma bleed as this man did. Benign adenoma can behave exactly like carcinoma, and the diagnosis can be made only by biopsy. It is my impression, however, that in most cases of adenoma there is complete obstruction, with atelectasis.

As in most tumors, the diagnosis without tissue examination is one of guesswork. I therefore make my guess that the most probable diagnoses were two independent conditions: neurofibroma, probably arising from the esophagus; and primary carcinoma of the right-lower-lobe main bronchus, with abscess formation behind the bronchial obstruction.

CLINICAL DIAGNOSES

Carcinoma of lung, bronchiogenic.
Bronchopneumonia, slight.

DR. PITTMAN'S DIAGNOSES

Neurofibroma, probably arising from esophagus.
Primary carcinoma, right-lower-lobe main bronchus, with abscess formation behind bronchial obstruction.

ANATOMICAL DIAGNOSES

Epidermoid carcinoma, bronchiogenic, of right upper lobe, with extension to esophagus, vertebrae and mediastinal lymph nodes.
Pulmonary abscesses, multiple, right upper lobe.
Empyema, right, massive.
Emaciation.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The contiguity of the upper respiratory and gastrointestinal tracts makes it comparatively easy for a malignant process arising in either to invade the other at a comparatively early stage of its development. Consequently, we see cancers of the lungs with the presenting symptom of dysphagia, and primary cancers of the esophagus in which the first symptom may be cough or hemoptysis. The picture is often further complicated by extensive secondary infection so that one is often faced with a double barreled problem, as Dr. Pittman was in this case and must try first to name the source of the neoplasm and secondly to localize the complicating infection. I do not believe in this case Dr. Pittman received the help from the roentgenologist that she might reasonably have expected. I am quite unable to make the facts determined at autopsy check with their recorded observations.

The primary lesion, as Dr. Pittman predicted was neoplasm, a carcinoma arising in the bronchus to the right upper lobe. It had grown downward along the right primary bronchus which was almost completely occluded. The tumor occupied approximately half the upper lobe and the lungs peripheral to it contained innumerable abscesses, one of them measuring 2 cm. in diameter. In contrast, the right lower lobe where the radiologist found evidence of extensive consolidation showed practically nothing but minimal acute terminal bronchopneumonia at the time of autopsy. There was also on this right side an extensive empyema consisting of nearly 2000 cc. of very turbid foul-smelling fluid. This unquestionably was a terminal event, and there was no evidence pointing to it in the recorded summary. The tumor had invaded extensively the posterior mediastinum and, in fact, had extended deeply into the two upper thoracic vertebrae. It had grown through the wall of the esophagus, and two intraluminal tumor masses were present to account for the esophageal obstruction. The mucosa over these was not ulcerated, however. Consequently the picture was not unlike that seen with an intramural leiomyoma or neurofibroma of the esophagus, as Dr. Pittman suggested. No distant metastases were found.

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WAR AND VENEREAL DISEASE

THIS country is at war, and venereal disease is on the increase. Just when the national campaign against syphilis and gonorrhea was beginning to bear fruit, there has been an upward turn in the incidence curve of these diseases, chiefly owing to an increase of the venereal-disease rate in the armed services. Every possible effort is being made to educate the men to avoid these diseases, and healthy activities to employ their spare time are provided. The Army and Navy Medical Corps and the United States Public Health Service are expanding their personnel as rapidly as possible to cope with the situation. Two outstanding problems in this field require the co-operation of practicing physicians.

The first concerns the situation in cities and towns near large encampments of men. The

efficient handling of prostitution and of syphilis and gonorrhea in the civil population requires the closest co-operation of the military and civil authorities and the physicians of the particular district. Provisions for the detection of new and old cases, for their quarantine and for adequate treatment and follow-up are taxing the resources of many communities. Somehow or other, the job must be done, to avoid the noneffectiveness that existed in the last war.

The second problem concerns the selectees who are excluded from military service because of evidence of syphilis or gonorrhea. Some of these 45,000 men from the first million selectees could undoubtedly be rendered fit for service, but they must be followed up and treated. Elsewhere in this issue of the *Journal*, Dr. Vonderlehr indicates that only half these men have been brought to treatment and that many communities have done comparatively little in the way of finding them. He points out, "If this opportunity is lost, . . . it will constitute one of the greatest public-health and medical failures in the history of the United States."

THE HERITAGE OF CONNECTICUT MEDICINE

THE Connecticut State Medical Society celebrated its sesquicentennial this year in June at Wesleyan University, with an appropriate program of general and historical interest and by the publication of *The Heritage of Connecticut Medicine*,* a volume containing a history of early medicine in the state and numerous essays on famous Connecticut physicians—William Beaumont, Horace Wells and the Doctors Welch—and the advances in medical teaching and practice, public health, psychiatry, physiology, surgery and tuberculosis as they have developed in Connecticut. Both the meeting and the book are outstanding contributions; Connecticut, with its first meeting of the state medical society in 1792, has indeed set an example that other states might well follow.

**The Heritage of Connecticut Medicine*. By various authors. Edited by Herbert Thoms, M.D. 223 pp. New Haven, Connecticut: privately printed for the Connecticut State Medical Society, 1912.

The beginnings of organized medicine in Connecticut go back well into the eighteenth century, since an attempt was made to obtain a charter as early as 1763. This failed but, in 1784, the New Haven County Medical Society was founded, and its famous transactions, *Cases and Observations*, printed in 1788, was the first medical publication in this country. It was not until October 9, 1792, however, that thirty-six practitioners of medicine gathered in the Court House in Middletown for the first meeting of the Connecticut State Medical Society. The names of these physicians have a familiar ring in New England medicine,—Hubbard, Munson, Potter, Tudor, Flagg, Mather, Coit, Clark, Lord, Woodward and others,—and not a few men bearing the same surnames serve Connecticut and the other New England states today.

Thus, the fourth state medical society to be established in America came into being; its past performance is great, and its future can be no less. Many should read, with pleasure and profit, the history of the illustrious past of this state medical society, and of the lives of the physicians who made it. The volume is worthy of the heritage presented on its pages, and shows that Connecticut doctors of our day have thoughtfully and wisely evaluated the work of their colleagues of the past.

MEDICAL EPONYM

PURKINJE FIBERS

These fibers were described by Professor Johann Evangelista von Purkinje (1787-1869), of Prague, in an article "Mikroskopisch-neurologische Beobachtungen [Microscopic-neurologic Observations]," published in the *Archiv für Anatomie, Physiologie und Wissenschaftliche Medizin* (681: 281-295, 1845). A portion of the translation follows:

On the inner walls of the ventricles of the sheep's heart, I observed, first with the naked eye, a network of gray, flat, gelatinous threads immediately beneath the serous membrane. . . . On microscopic examination, I found these threads to be entirely made up of granules. . . . Inside each granule, there were one or two nuclei without any spherical envelope such as is seen in true ganglion cells. The fibers were formed of cross rows of five or ten of these granules, arranged serially in bundles.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY: FATAL ECLAMPSIA

A thirty-eight-year-old multipara had had adequate though unintelligent care during her ninth pregnancy. Her previous pregnancies had been normal, and the past history was irrelevant. At the beginning of this pregnancy, the blood pressure was 150 systolic, 90 diastolic; the systolic blood pressure rose to 170 during the last two months. The patient had been seen every two weeks from the third month of pregnancy, and the urine was reported to be normal. In the last month of pregnancy, she was seized with a sharp pain under the right shoulder, for which she was given $\frac{1}{4}$ gr. of morphine. Two or three hours later, she began to flow and had a convulsion, which was the first of several that occurred before she entered the hospital. The day after entry, she delivered herself of a stillborn baby. There was no post-partum hemorrhage, but she had one convulsion after the birth of the child. Examination of the blood showed a steadily rising nonprotein nitrogen; almost complete anuria developed, which resulted in death ten days after delivery.

Comment. This death was undoubtedly an unnecessary obstetric fatality. Any patient who starts a pregnancy with a systolic blood pressure of 150 that reaches 170 at seven months and continues at that elevation should probably never be allowed to go to term. After the convulsion, nothing could have been done that was not done to ensure recovery. Induction any time after the beginning of the last month, either by rupture of the membranes or by the use of a Voorhees bag,—preferably the former,—would have saved the mother's life and probably prevented the death of the baby.

Routine visits on patients of this sort do not necessarily mean intelligent obstetrics. This patient had routine care; it was not, however, intelligent.

DEATHS

BRYANT—ALICE G. BRYANT, M.D., of Boston, died July 25. She was in her eighty-first year.

Born in Boston, Dr. Bryant received her degree from Woman's Medical College of the New York Infirmary for Women and Children in 1890. She was associated with Vincent Memorial Hospital, New England Hospital for Women and Children and New England Deaconess Hospital. She was a member of the American Academy of Ophthalmology and Oto-Laryngology, and a fellow of the Massachusetts Medical Society and the American Medical Association.

BURNETT—N LOWE BURNETT, M.D. of Cambridge, died July 20. He was in his fifty sixth year.

A native of Springfield, Dr. Burnett received his degree from Queen's University Faculty of Medicine in 1915. He was president of the Bay State Medical Association, and a former member of the Massachusetts Medical Society and the American Medical Association.

His widow, three sons and a daughter survive him.

FROTHINGHAM—CHARLES B. FROTHINGHAM, M.D., of Lynn, died May 28. He was in his eighty fifth year.

Dr. Frothingham received his degree from Dartmouth Medical School in 1892. For many years, he was city physician in Lynn and a member of the school committee. He was a former member of the Massachusetts Medical Society.

GLIDDEN—HOWARD K. GLIDDEN, M.D., of Swampscott, died May 30. He was in his sixty eighth year.

Dr. Glidden was a former member of the Swampscott Board of Health, and a former member of the Massachusetts Medical Society and the American Medical Association.

MORSE—ALMON G. MORSE, M.D., of Hingham, died July 27. He was in his seventy fifth year.

A native of Watertown, Dr. Morse received his degree from Harvard Medical School in 1894. He served as house officer, assistant surgeon and surgeon in chief at the Massachusetts Eye and Ear Infirmary. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, two sons and a daughter survive him.

STACK—CHARLES F. STACK, M.D., of Hyde Park, died April 3. He was in his seventy second year.

Born in Hyde Park, Dr. Stack received his degree from Harvard Medical School in 1898. He served his internship at Boston City Hospital and did postgraduate study in Europe. He was a member of the Massachusetts Medical Society and the American Medical Association.

A son and a daughter survive him.

WAR ACTIVITIES

CIVILIAN DEFENSE

The following memorandum was recently issued by the Office of Civilian Defense, Washington, D. C. regarding the relation of emergency medical services to industrial plants.

* * *

The primary responsibility for the protection of industrial plants rests on the operators, owners, and local and state governments. The War and Navy departments have included in their protective program the responsibility for surveying and recommending protection within certain civilian manufacturing plants engaged in the production of war materials, as well as for plants owned and operated by these departments. The emergency medical services provided in these plants and in all other plants should be closely integrated with the local emergency medical services. The War and Navy departments have requested all civilian manufacturing plants having important war contracts to co-operate with the local emergency medical service of the United States Office of Civilian Defense. All local chiefs of emergency medical services should be prepared to co-operate with the man-

agements of plants having important War and Navy contracts whenever requested, by responsible officials within the plants, to do so.

All industrial plants are expected to provide medical services and first aid equipment within the plant for the care of the injured. In the event of enemy action directed against such industrial plants, the physicians, nurses and first aid detachments within the plants may be inadequate to care for the serious injuries produced by high explosives or incendiaries. It is the recommendation of the Office of Civilian Defense that each industrial plant, in addition to providing its own medical staff and first aid equipment, should plan in collaboration with the chief of emergency medical services of the locality for services of ambulances, when needed, available beds at one or more hospitals, to which the severe casualties may be transported, the establishment of a casualty station of the emergency medical service within a short distance of the plant, and the services of emergency medical field units, if needed to supplement the plant medical service during an emergency.

In view of the fact that enemy action against industrial plants may be coincidental with widespread damage to the adjacent community, the mobilization of civilian medical resources during an emergency will be accomplished through the commander of the citizens' defense corps.

If a plant is miles from a hospital and there is, therefore, a possibility that the injured may be obliged to remain at the casualty station for many hours before being transferred to the hospital, the casualty station should be larger than the average for a given number of employees and be adequately equipped. It must have cots, blankets, water and heating facilities, and be equipped at least with the emergency medical supplies.

MISCELLANY

NOTES

Thirty three appointments to the teaching and research staffs of the Harvard Medical School, effective July 1, were recently announced by Harvard University as follows:

Assistants in surgery Robert K. Brown, of Colorado Springs, Colorado, M.D. Harvard '37, Richard C. Durant, of Great Barrington, Massachusetts, M.D. Harvard '34, Howard A. Frank, of Woodmere, Long Island, New York, M.D. New York University '37, John J. Lowrey, of Honolulu, M.D. Harvard '40, Donald D. Matson, of Altadena, California, M.D. Harvard '39, Arnold Porter, of Providence, Rhode Island, M.D. Harvard '40, Frank R. Pierce, of Gardner, Massachusetts, M.D. Harvard '34, Carter R. Rowe, of Fredericksburg, Virginia, M.D. Harvard '33, Eric R. Sundersen of Boston, M.D. Harvard '37, Neal W. Swinton, of Waban, Massachusetts, M.D. University of Michigan '29, and Lester P. K. Yee, of Honolulu, M.D. Harvard '37.

Assistants in medicine Howard E. Allen, of Salt Lake City, M.D. Pennsylvania '38, and Samuel Stearns, of Dorchester, Massachusetts, M.D. University of Michigan '39.

Research fellows in medicine Grosvenor W. Bissell, of Buffalo, New York, M.D. University of Buffalo '39, William C. Bridges, of Tacoma, Washington, M.D. Yale '40, Harry A. Feldman, of Newark, New Jersey, M.D. George Washington University '39, Seymour S. Kety, of Philadelphia, M.D. Pennsylvania '40, Charles R. Park, of Garrison, Maryland, M.D. Johns Hopkins '41, and Edward

C. Reifenstein, Jr., of Syracuse, New York, M.D. Syracuse '34.

Assistants in gynecology: John R. Barker, of Waban, Massachusetts, M.D. Tufts '31; and Charles L. Sullivan, of Brookline, Massachusetts, M.D. Boston University '35.

Teaching fellows in bacteriology and immunology: Charles A. Macgregor, of Rumford, Maine, M.D. Harvard '42; and James H. Strauch, of Canton, Ohio, M.D. Harvard '42.

Instructors in nutrition: David M. Hegsted, of Chicago, Ph.D. Wisconsin '40; and John M. McKibbin, of Madison, Wisconsin, Ph.D. Wisconsin '42.

Visiting lecturer on anatomy: William C. Young of New Haven, Connecticut, Ph.D. University of Chicago '27.

Instructor in anatomy: Richard J. Blandau, of Providence, Rhode Island, Ph.D. Brown '39.

Teaching fellow in anatomy: Macelyn V. Anders, of Marietta, Ohio, S.M. Brown '42.

Assistant in bacteriology and immunology: John B. Hamblet, of Lowell, Massachusetts, M.D. McGill '40.

Assistant in roentgenology: Lloyd E. Hawes, of West Somerville, Massachusetts, M.D. Harvard '37.

Assistant in psychiatry: James E. Roy, of Worcester, Massachusetts, M.D. Harvard '39.

Assistant in neurology: Frederick G. Woodson, of University, Virginia, M.D. University of Virginia '38.

Instructor in pathology: Clinton Van Z. Hawn, of Albany, New York, M.D. Harvard '41.

Dr. Harris P. Mosher, professor of laryngology and otology, emeritus, at Harvard Medical School, was awarded an honorary degree at the recent commencement exercises of Jefferson College, Philadelphia.

Dr. Reginald Fitz, lecturer on the history of medicine and assistant to the dean, Harvard Medical School, recently delivered the commencement address at the University of Vermont College of Medicine.

Dr. Frederic A. Gibbs, of Boston, was recently elected secretary-treasurer of the American Branch of the International League against Epilepsy.

Fifteen members of the first-year class at Tufts College Medical School were recently awarded Charles Hayden Memorial Scholarships of \$250 each. Dr. Cadis Phipps, chairman of the scholarship committee and head of the Department of Medicine, distributed certificates denoting the awards. The recipients were as follows: John J. Carty, of Jamaica Plain; Francis L. Colpoys, Jr., of Brighton; Harvey H. Corman, of Dorchester; Francis X. Mack, of Milton; Edward Martin, Jr., of Milton; John A. McGowan, of Medford; John C. McLaughlin, of Brookline; Willard Nicholl, of Needham; Emil Pagliarulo, of East Boston; Vincent P. Perlo, of Brookline; Harold S. Rubin, of Swampscott; Robert J. Scannell, of Brighton; Stuart A. Silliker, of Cambridge; Richard E. Stiles, of Roslindale; and Francis A. D'Ambrosia, of Boston.

CORRESPONDENCE

LEGAL ASPECTS OF FIRST AID

To the Editor: I have been greatly interested in the work that is being done in training groups of laymen in first aid. But neither in the courses for air-raid wardens nor special police, which I have attended, in the course for physicians given by the Massachusetts Committee on

Public Safety nor in any publication have I seen any reference to the medicolegal aspect of first aid.

These men and women, who are giving their time and energy to prepare for the emergencies that seem more inevitable day by day, deserve nothing but commendation. They are doing a fine piece of work, of which the public, including the medical profession, knows too little. If, as a result of their efforts to care for air-raid victims, they are to incur the risk of becoming defendants in lawsuits, brought by disgruntled "victims" whom they have attended, the fact should be known, so that they may be informed concerning both the extent of the risk and the means at their disposal for avoiding such liability or of meeting it when it comes. Physicians know that it is idle to rely on the gratitude or sportsmanship of patients for protection from lawsuits, and it is not likely that these laymen would find themselves in any better position in the event of some unforeseen catastrophe.

CHARLES E. WELLS, M.D.

15 Union Street
Randolph, Massachusetts

* * *

Dr. Wells was referred to an article, "Legal Aspects of First Aid by Lay People," in the June, 1942, issue of *Minnesota Medicine*. Since the laws governing such actions vary from state to state, the *Journal* will attempt to obtain an opinion concerning the legal aspects of first-aid care in Massachusetts. — Ed.

REPORTS OF MEETINGS

NEW ENGLAND PEDIATRIC SOCIETY

A regular meeting of the New England Pediatric Society, with Dr. Warren R. Sisson presiding, was held at Longwood Towers on March 25.

The first speaker was Dr. Richard M. Smith, whose talk was entitled "Protection of Children in Wartime." Definite problems are precipitated in the danger zones of the seaboard and areas near defense industries or military targets. It has been generally agreed that the registering of all children in such areas is advisable and feasible, but although the Office of Civilian Defense recognizes these facts the priorities board states that no metal is available for tags. And to be effective, registration must be done on a national scale. In evacuation of any of these zones, children are the first priority group, and the plans for their removal in an emergency are already under way in most communities. The only question that arises is the feasibility of carrying out such evacuation prior to the expected incident.

The problem of general immunization against communicable diseases is always present. Proclamations have been issued making smallpox and diphtheria prophylaxis mandatory, but it is generally believed that at least tetanus should be added to this list. The camp movement should be extended, not only to provide "war vacations" but also to afford much-needed experience in mass evacuations.

The psychologic reactions of children to war are multiple and complicated, and by no means insignificant. Even toddlers feel the insecurity and actually experience fear. The problem in older children and adolescents is equally acute, and may be associated with even more serious consequences. The number of delinquencies and misdemeanors rises sharply, and such a possibility is being given the greatest attention in this country, following the sad experiences of England early in the war. This problem,

as well as others, is greatly accentuated by the rapid growth of such communities as newly created defense centers. Some areas have already experienced 1000 per cent increases in population. This introduces problems in housing and sanitation and all the difficulties entailed in quarters composed of trailers and improvised shacks. The need for medical care far outstrips the ability of the doctors to handle it. School facilities, in both material and personnel, soon become greatly overburdened, and it is freely predicted that all rural schoolteachers who are not already in war industry soon will be. Child labor again rears its head and the percentage of children employed is already rising sharply in many communities. Home life is disintegrating with the increase of men in various branches of the armed forces and of mothers in war industries. The absence of men leads to a great sense of insecurity. These facts have heightened interest in day care for children. Another potent factor, of course, is the high percentage of early divorces following hasty war marriages, which leave children essentially orphans.

In general, a concerted effort should be made to maintain the standards of child health so far as possible, with concessions only on a temporary basis if absolutely necessary and, then, with the least harm to the children. Furthermore, new and emergency methods should be developed to meet the particular situations arising from the war.

The second speaker of the evening was Dr. Joseph Stokes of Philadelphia, whose subject was "Communicable Diseases in Army Camps." This was essentially a report of the work of the Board of Communicable Diseases, especially regarding measles and mumps. Although there is a great need in wartime for control of these conditions, an ideal opportunity for investigation is also afforded. During the last war, there were 98,000 cases of measles with about 40 per cent mortality, and in the 40,000 cases of mumps, the incidence of orchitis varied from 5 to 40 per cent.

In the treatment and prophylaxis of measles, there is a crying need for large amounts of placental extract or pooled immune serum. One advantage of Cohn's albumin in the treatment of shock is the saving of large quantities of globulin, which may be useful in this role. Experiments are now in progress to test the efficacy of this fraction against some viruses, but more study is necessary. At the Army Medical School, there is now a central collecting depot for immune serum. Passive immunity is obviously of no use except on hospital wards for it lasts only two or three weeks. It is practical, however, when non-immune patients are on a ward after exposure or are being sent on active duty following a measles outbreak in camp. The sulfonamides are being employed in alternate cases of measles for investigative purposes.

Since the virus of measles has been isolated from the brain of a person dying of measles encephalitis, it is considered advisable to treat such patients early with massive doses of convalescent serum. Similar therapy, consisting of as much as 150 to 200 cc in children, may modify or even prevent the rash of measles if inaugurated as soon as Koplik spots are noted. To decrease the ever-present danger of cross infections, the use of propylene glycol vapor and ultraviolet light is being tried in camps. The only study so far on mumps has been the treatment of alternate patients with convalescent serum to determine its effect on the incidence of orchitis. The use of serum in one series and of incision in another, on alternate cases, is being contemplated. In mumps encephali-

tis, the virus may also be involved, but the treatment of alternate cases is probably impracticable because of the small number of cases. So far, there have been more cases of mumps than measles, but both diseases have been relatively low in incidence. As a preliminary report, there is a favorable feeling toward the effect of serum on orchitis. The question that there may be some synergistic action of the gonococcus on mumps orchitis has led to the proposal of sulfonamide treatment.

One of the most important interim investigations on measles virus concerns the value of active immunization. In 1935, this virus was first grown on the chick embryo but there were no studies on transmission in man or monkey until Plotz passed it in successive steps from the embryo to monkeys and back. The virus could be obtained from both the nose and the blood. Shafer et al. exposed human subjects to measles virus following immunization with virus attenuated on chick embryos. Children and monkeys injected with the latter material develop Koplik spots, neutrophilopenia and only rare skin eruptions, which are of a mild nature. Although there is some fever the malaise is not comparable to that of the usual case, and cough is rare. The resulting disease is even less severe than the attenuated normal disease or that modified by convalescent serum. Of 217 children inoculated with this attenuated virus, only 10 per cent on subsequent exposure contracted moderately severe measles, whereas in the rest the disease was mild or minimal or did not occur. The virus was administered intranasally and intradermally with essentially no difference in results, with the possible exception that intranasal administration seemed to cause some Koplik spots. In another series in which 43 nonimmune subjects were exposed to measles, 25 of the 36 untreated ones developed measles, whereas none of the 7 immunized persons developed the disease. A challenge inoculation of blood from patients with active measles into 15 such actively immunized children resulted in only 5 cases of the disease, 2 of which were modified.

Many years of study are necessary to settle the efficacy of this attenuated virus. There is need for better titration methods, monkey neutralization being the only present means of standardization. Whether to use this in the army is still debatable, since there is still some suggestion that the virus may be reactivated by human passage.

GREATER BOSTON MEDICAL SOCIETY

At a regular meeting of the Greater Boston Medical Society held at the Beth Israel Hospital on April 7, Dr. Samuel Silbert discussed "Recent Advances in the Treatment of Peripheral Vascular Disease."

As standard therapy for peripheral obliterative arterial disease the most important single measure is the absolute abstinence from the use of tobacco. Hypertonic saline solution intravenously was employed in 517 cases of thromboangitis obliterans, 96 per cent of which, when once cured, remained asymptomatic for two to eighteen years if smoking was discontinued. It has been concluded, therefore, that tobacco causes thromboangitis obliterans and that treatment affords excellent results if smoking is stopped.

For the relief of pain, the results have been somewhat less striking. Typhoid vaccine has resulted favorably in many cases, but may be dangerous. Five million bacteria are administered in the first dose, and double that amount at each subsequent injection. This form of therapy is not employed in patients over sixty years of age or when the temperature is more than 101°F. Division of the

sensory nerves of the foot was advocated early in the study of the condition, but should properly be reserved for cases not controlled by the usual sedatives or foreign-protein injections, and also only if there is an intractable ulcer. Otherwise, gangrene may ensue. Nerve block has now superseded division, if either is indicated.

Many methods have been suggested to increase the collateral circulation. Since 1922, at Mount Sinai Hospital in New York City, hypertonic saline solution has been routinely injected in 800 obliterative cases. During that period, major amputations have decreased from 62 to 7 per cent. Although the strict adherence to the no-tobacco rule has undoubtedly favorably influenced these statistics, the percentage of amputations is still much smaller than that at other large clinics. This is not claimed as a specific form of therapy, and it may be employed in arteriosclerotic cases. It should be avoided, however, in patients over sixty-five years of age, in cardiac patients and in nephritic patients. Sympathectomy, which was the result of an astute side observation during operations for spastic paralysis, has been employed in increasingly larger series of cases. This operation removes the normal sympathetic vasoconstrictor activity and, in many cases, increases the temperature and the circulation in the affected extremity. However, Dr. Silbert claims no improvement in walking by decrease of the claudication. He has observed no remarkable change in temperature in the muscles on sacral block, spinal anesthesia or sympathectomy. It is concluded that the circulation is not equally increased in all tissues and that this method is adequate for healing indolent ulcers but not for decreasing claudication. On the other hand, the administration of 300 cc. of 5 per cent saline increased the temperature in all tissues of the extremity. A third general method of increasing collateral circulation is the use of venous stasis of some sort. This also is advantageous only in healing stubborn ulcers. This work resulted from war surgery, which demonstrated that if an artery had to be ligated or sacrificed, the limb was much less apt to develop gangrene if the accompanying vein was divided. It allows some nutrition of the otherwise starved tissues. The three commonest methods of accomplishing venous stasis are: the pavex boot, which rhythmically changes the pressure from -80 to +20 mm.; intermittent venous occlusion, which can be conveniently carried out with an ordinary blood-pressure cuff; and the Sanders oscillating bed, which rhythmically changes the position of the lower extremities in relation to the rest of the body.

Dr. Silbert stated that, at his clinic, varicose veins of the leg are now treated by injection rather than by division of the lower branches, an original high saphenectomy having been carried out.

One of the most striking and highly publicized recent advances is that of the employment of cold in peripheral vascular disease. The initial use of warmth in vascular occlusion is now definitely outmoded. Heat not only increases the circulation to a part but also increases the tissue metabolism and oxygen demand. But when the vessels are unable to respond by vasodilatation and the metabolism increases, the tissues merely have their anoxia accentuated. Local heat in proper amounts, however, is beneficial, and a maintenance of a temperature of 95°F., regulated with a thermostat, is now being employed in the chronic stages of vascular disease. In a rapid decrease of blood flow, such as occurs in embolism, cold in the form of ice bags should be immediately applied to the part. Cold has never been observed to do harm when properly used. Later, mild heat should be applied to increase the collateral circulation. Cold may also be used

advantageously in many cases as a temporary expedient to allay the pain of sudden vascular occlusion.

Another recent advance is the use of heparin to decrease a thrombotic tendency. Derangement of this tendency causes a great increase in surgical mortality, and the management is complicated by the fact that the emboli and thromboses may be multiple, since one is dealing with a tendency. In fact, thromboses cause 6 per cent of all surgical deaths. The proper use of heparin costs ten to fifteen dollars a day for the necessary 250 to 350 mg. It is usually best administered by the continuous intravenous route in physiologic saline solution. It prolongs the coagulation time, but to a variable degree in different people and in the same person at different times. It is used clinically to prevent postoperative venous thrombosis and arterial thrombosis following embolectomy, accidents and so forth, and in the treatment of pulmonary emboli postoperatively and post partum, to aid thrombophlebitis and to decrease central retinal and coronary thrombosis.

Statistics at the Mayo Clinic indicate that 0.7 per cent of all operations, 1.6 per cent of laparotomies and 2.7 per cent of pelvic operations develop thromboses postoperatively. On that basis, Murray, in Toronto, should have had four thromboses in his 400 cases in which he used heparin routinely postoperatively, but there were none. Dr. Silbert is of the opinion that emboli are not apt to occur when swelling or other inflammatory signs accompany the thrombosis. Heparin may be especially helpful in preventing subsequent emboli in a person who has had a nonfatal one. This substance is far too expensive for general use, and the need for some reasonably priced anticoagulant is evident. A possible solution to this dilemma may be Dicoumarin, a compound discovered and synthesized in 1941 but not as yet commercially available. This substance is effective orally and is administered in doses of 50 to 200 mg. about every two days. The coagulability of the blood is usually not affected for several days, and heparin may be temporarily used at first. The effect also persists for several days after cessation of therapy. The incidence of hemorrhage has been greater than that with heparin at the New York hospitals. Treatment of this complication is by repeated blood transfusions. Prothrombin times should be closely followed, needless to say.

There have been promising developments in nonobliterative arterial disease. In Raynaud's disease, Smithwick's modified preganglionic sympathectomy seems to offer hope of relief. Spiegel considered Raynaud's disease a general metabolic disorder and has shown striking results with the use of diets high in vitamin B. This, of course, cannot affect the irreversible changes of associated scleroderma. Some improvement has been claimed following the use of dihydrotachysterol.

Dr. John Homans opened the discussion by offering some views of one of the Boston schools of thought. Hypertonic saline solution has shown no such striking results, whether because of insufficient intensity or duration of treatment. It has been claimed that no increase of circulation can be demonstrated following its use. The Massachusetts General Hospital group claim improvement by a properly executed sympathectomy in any arterial disease, but Dr. Homans agrees that only limited cases are benefited. Tobacco deprivation is undeniably the best of all treatments for thromboangiitis obliterans. The prevalent fungous infections of the feet, however, should be intensively treated, for they may not only complicate but even have some etiologic role in this condition. Complete agreement was voiced with the speaker's opinions

on the use of heat and cold, except in cases of thrombosis, in which Dr Homans believes in moderate heat in an attempt to increase the circulation. He is frankly scared by the not infrequent occurrence of deep and wandering thrombophlebitis following even the gradual and careful withdrawal of heparin. He does not accept Murray's statistics.

Dr E. Everett O'Neil was not sure of the results with hypertonic saline solution. However, sympathectomy is the quickest and most permanent method of increasing the vascular bed in the greatest number of patients in his hands. There is enough spastic element even in the most characteristic obliterative disease to warrant surgical denervation. Twenty-eight per cent of 40 patients had relief of intermittent claudication following sympathectomy. Cold certainly does symptomatically improve both acute and chronic obliterative arterial disease. Refrigeration and the application of a tourniquet have been followed by amputation in two to ten hours, with a great decrease in the amount of shock, bacterial activity and pain. This has been entirely a poor risk group in whom the mortality has been thus lowered from 100 to 50 per cent, largely because of the decreased shock, and lack of anesthesia. These mortality data are almost as good as those from many clinics with selected cases. As for heparin and Dicoumarin, he would rather use femoral ligation if the thrombosis can be located. It is no longer necessary except when the site of the thrombosis is hidden. Besides the slowness of its effects, hemorrhagic reactions of Dicoumarin may not respond to transfusions.

Dr John Sears congratulated Dr Silbert on being able to enforce his no smoking rule so successfully. He has been impressed by the number of patients in Dr Silbert's clinic who have open lesions but no pain. One interesting group at the Beth Israel Hospital are the patients with definitely proved thromboangitis, who are now "burned out" and are asymptomatic despite their continued smoking. Since August, 1939, division of the femoral or iliac vein has been immediately carried out as soon as the diagnosis of a deep thrombosis is made. Heparin and Dicoumarin are considered expensive and dangerous.

In conclusion, Dr Silbert emphasized the fact that tobacco is the one proved factor in thromboangitis obliterans. Ice bags should be used only for pain, and the extent of their use controlled by the patients' reactions. This does not preclude the use of immediate embolectomy or vein division if the indications are clear. Heparin withdrawal is admitted to entail definite dangers. Sympathectomy may benefit partly by its psychic effects.

BOOK REVIEWS

The Retina. The anatomy and the histology of the retina in man, ape and monkey including the consideration of visual functions, the history of physiological optics and the histological laboratory technique. By S. L. Polyak, M.D. A fiftieth anniversary publication of the University of Chicago Press. 4th, cloth, 729 pp., with 100 illustrations. Chicago: The University of Chicago Press, 1941. \$10.00.

Nine years of original research in the primate retina and visual pathways are recorded in this volume, whose counterpart, "The Visual Pathway," is now in preparation by the same author.

Three fifths of the book is devoted to a discussion in five sections of methods of investigation, history of visual structure and function from early Greek and Arab times down through European studies to the present time, study of the minute structure of the retina, and an interpretation of function in terms of structure, especially of the

neuroepithelium, the conducting fibers and the synapse. Two fifths of the text is devoted to a general outline, to one hundred full page illustrations amply labeled, to one hundred and twenty nine pages of bibliography and to a full index of contents.

This work must be read to be appreciated, and is an authoritative and stimulating work. It should have its place in the working library of every neurophysiologist, neuropathologist, neurologist and ophthalmologist, especially if such a specialist is engaged in research work or teaching. It is one of the outstanding books of the year in the field of ophthalmology.

Hugh Young. A surgeon's autobiography. 8°, cloth, 567 pp., with 91 figures and 18 portraits. New York: Harcourt, Brace and Company, 1940. \$5.00.

This autobiography covers seventy years of the striking and somewhat unusual career of a urologist, one of the better known physicians in recent American medicine. An unusual feature of the volume is the inclusion of details of the author's medical work, a section covering about one fifth of the whole book. Over one hundred pages are virtually a textbook of urology, with numerous drawings of surgical operations and urologic instruments. Since Dr. Young was primarily a surgeon, who pioneered in his specialty, he gives the complete story. He justifies his decision in the preface, by writing "Urology was too important a part of my life to be omitted. That would be sacrificing the true picture." He elected to tell the most important happenings in his medical career, exactly as he would narrate any other event of interest to him. The anatomic and surgical drawings are remarkably clear and labeled so that they can be viewed with understanding by an intelligent layman.

The rest of the story is somewhat less striking. His early life in Texas and at the University of Virginia is well told, but physicians will welcome most his notes on the early days of the Johns Hopkins Hospital, with fleeting pictures of Finney, Osler, Welch, Flexner and, particularly, Halsted. There are no deep characterizations, only touches, leaving one with a desire for more.

Young's later life was one of great activity—in the A.E.F. and in Maryland, where he was energetic in fostering legislation for the control of tuberculosis and the care of the insane. He traveled abroad extensively, and many chapters are devoted to his trips and his interest in sports.

In general, the book is interesting, for the author led a colorful life. There is, however, in the reviewer's opinion, little brilliance and some bad taste. Through it all runs the fixed purpose of advancing urology, and to those particularly associated with this special field of surgery, the book will serve as a milestone in that advance. To others, the book offers some basic material to round out the history of medicine in America.

Subacute Bacterial Endocarditis. By Emanuel Libman, M.D., and Charles K. Friedberg, M.D. Edited by Henry A. Christian, M.D., LL.D., Sc.D. (hon.), F.A.C.P., F.R.C.P. (Can., hon.). Reprinted from *Oxford Loose Leaf Medicine* 8°, cloth, 108 pp., with 19 illustrations. London: Oxford University Press, 1941. \$2.75.

When a physician makes a diagnosis of subacute bacterial endocarditis, he realizes that, at the moment, there is little he can do to help the patient. In view of the rapid advances, however, that have been made by modern chemotherapy, he always looks forward to the time

when some really effective form of therapy for this disease will be devised. And, at such a time, he must be able to recognize the disease in its early stages, when the vegetations are small and before extensive and irremediable structural damage to the tissues has occurred. Consequently, it is gratifying indeed to have this excellent monograph. With the mastering of most of the facts of this book, a physician should find little difficulty in making an early diagnosis. Furthermore, the authors will bolster the morale of the physician, since they state that about 4 per cent of all known cases have a favorable result owing to spontaneous recovery.

This book will also enable the physician to develop a critical estimate of the current literature on the subject. The monograph covers the disease thoroughly, for it is written by well-known clinicians who are keen observers. It also reveals the authority that comes from a wide personal experience, since Dr. Libman himself has personally observed at least 1000 cases from 1899 to 1930.

To review this monograph fully would require a brief summary of every page, because the work is saturated with facts. The bibliography is complete and up to date.

This study should be of value to every clinician. It is also a model for one to follow in the writing of a medical monograph.

Synopsis of the Preparation and Aftercare of Surgical Patients. By Hugh C. Ilgenfritz, M.D., and Rawley M. Penick, Jr., M.D. With a foreword by Urban Maes, M.D., D.Sc. 12°, cloth, 532 pp., with 55 illustrations. St. Louis: The C. V. Mosby Company, 1941. \$5.00.

The subject of preoperative and postoperative care was formerly included in the introductory chapters of volumes on surgery. This minor emphasis was in large part responsible for the aphorism that "the operation was successful, but the patient died." The increasing interest in the care of the patient before and after operation is in large part responsible for the reduction in surgical mortality.

This volume is unusually compact, and its size belies the wealth of information that it contains. The opening chapters are devoted to such general considerations as fluid and electrolyte balance. The major and minor complications of surgery are considered in some detail. In addition to the treatment of these conditions, the authors include prophylactic measures that can be taken for their prevention. Finally, there are problems of care peculiar to biliary, thyroid, colonic and other types of surgery.

The authors are to be commended for their editorial policy. The book is easy to read because of the simple manner in which all the material is presented. It is a book that medical students will understand readily and practicing surgeons will find most helpful in the solution of their problems.

Essentials of General Surgery. By Wallace P. Ritchie, M.D. 8°, cloth, 813 pp., with 237 illustrations. St. Louis: The C. V. Mosby Company, 1941. \$8.50.

This book, with a foreword by Wangenstein, and with several chapters in special fields written by the author's colleagues, is apparently intended as an introductory textbook of surgery for students at the University of Minnesota Medical School. General principles are stressed, and operative procedures are wisely omitted. The objectives of the author consist "in acquainting students with the fundamental principles of surgery, in instructing them in methods which will enable students to recognize surgi-

cal disorders, and finally in teaching them what surgery can accomplish in the treatment of various diseases."

Numerous paragraph headings and subheadings, outline and tabular presentations, and elimination of much discussion of alternative methods of therapy have permitted condensation of the text to a remarkable degree. This condensation has resulted in didacticism in many cases, with omission of necessary relevant discussion and explanation. Thus, the chapter dealing with fractures refers to the Jones sling, the Bellevue splint, Buck's extension, Pott's fracture, Whitman plaster, Maxwell-Ruth traction and the Roger-Anderson method, but there is no description or explanation of what is meant by these terms.

Selected references chiefly to current literature are given at the ends of the chapters, but there is no authors' index, and the student will not find references to such fundamental contributions as Halsted's on carcinoma of the breast, although there is a brief allusion to Halsted's radical mastectomy.

In the main, the text is well written and clear, the illustrations are adequate, and the typography and the format of the book are pleasing.

NOTICES

UNITED STATES CIVIL SERVICE EXAMINATIONS

Junior Medical Officer (Rotating Internship) \$2000 a Year
Junior Medical Officer (Psychiatric Resident) \$2000 a Year

The Civil Service Commission has announced that positions are available for junior medical officer (rotating internship) and junior medical officer (psychiatric resident) in St. Elizabeth's Hospital for the treatment of mental disorders, Washington, D. C. Applications will be accepted until the needs of the service have been met, and appointments will be known as war service appointments.

The duties of the rotating internships are as follows: under immediate supervision, to admit patients, take histories, make physical examinations and record findings; to make ward rounds of inspection, note charts and record observations; to prescribe for minor ailments or acute emergency cases; to dispense medicine in emergencies; to perform minor surgical operations; to assist at major operations and in redressing; to administer anesthetics; to make routine laboratory tests and analyses; to assist at outpatient clinics in dressing and in administering vaccines; and to keep records, make up case histories and compile statistics requiring medical training. To qualify for this position, applicants must have successfully completed a four-year course in a Class A medical school before the date of appointment.

The duties of the psychiatric residents are as follows: to take histories; to make physical and mental examinations and record the findings; to make rounds of inspection; to make notes; to prescribe for and treat minor ailments; to answer correspondence relative to patients; and to assist the chief of the service in all administrative and professional duties. To qualify for the position, applicants must have successfully completed their fourth year of study in a Class A medical school subsequent to December 31, 1936, and must have the degree of either B.M. or M.D. In addition, they must have successfully completed a rotating internship of at least one year.

No written examination will be required. Qualifications will be judged on the extent of experience, education and training. Applicants must be citizens of or owe allegiance to the United States, and must be physically capable

(Notices continued on page ix)

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DIAGNOSIS OF ALLERGIC STATES IN SELECTEES*

ROBERT W. HYDE, M.D.†

BOSTON

THE correct diagnosis and classification of allergic states in selectees have been difficult problems ever since the beginning of the induction-board examinations of the United States Army. Speed is a necessary component of these examinations, and the Army physicians have not always had such unlimited time, comparatively, in which to elicit and record an accurate history as their civil colleagues usually have. Furthermore, both positive and negative malingerers are occasionally seen, still further adding to the diagnostic difficulties. The examiner is therefore often faced with an unverified history of bronchial asthma and normal chest findings, but may be unable, in the limited time, to arrive at a correct, definitive diagnosis. Moreover, in a proved allergic case, it is often difficult to decide whether the condition is severe enough to warrant rejection for full military service.

In view of these diagnostic difficulties and with an eye to the future, a study of the allergic states has been made at the Boston Induction Station, with the hope that others may profit thereby.

Crandall,¹ in 1940, pointed out the gravity of the problem of allergy in the armed forces and the necessity for a complete history, and stressed the assistance expected of induction boards in eliminating the obvious cases, thereby lessening the load that would be placed on Army physicians in the subsequent treatment of men with mild cases who were accepted.

Regarding the desirability of disqualifying for general military service applicants with bronchial asthma of the mildest and most infrequent degree, evidence is available that such men are likely to be a source of future disability. In a recent paper, Andrus² points out the frequency of emphysema in men under forty in the Canadian Forces, with asthma as one of its presumptive causes. He notes

that even candidates accepted for service because of good general condition and lack of, or nonadmission of, symptoms became respiratory casualties, with an unfavorable course and ultimate discharge; such men have a tendency toward frequent illness and relapse, and form a reservoir of compensation seekers.

It is known that the patient with respiratory allergy has a higher average incidence of residual illness after being subjected to the lung irritants of chemical warfare, and medical officers have been particularly impressed with this fact. The hypersensitive respiratory tract is more easily injured than the normal by any lung irritant, and an aggravated form of a previously mild asthma often occurs, with the eventual development of chronic bronchitis, bronchiectasis and emphysema.

Army regulations specify that chronic diseases discovered in the first six months of service should be considered as having existed prior to entry into military service, thus relieving the Government of allowing compensation in such cases. Mild, infrequent asthma often does not manifest itself in the first six months of service, since the precipitating influences of seasonal pollens or infection may not be present. Hence, there is more risk of compensation than in other conditions, such as orthopedic defects, peptic ulcers and psychopathic states, that usually manifest themselves earlier. It seems clear that the allergic states deserve serious regard when an applicant for the Army is being considered.

The allergic states were not clearly understood as one disease until Cooke and Vander Veer³ showed that a large percentage of patients with asthma had histories of eczema, urticaria, angioneurotic edema and abnormal reactions to various foods. Therefore, all the older statistics, so far as the armed forces were concerned, refer only to bronchial asthma. Even with this lack, they show the importance of the problem in the past and furnish a basis for an estimate of the prevalence of

*From the Boston Recruiting and Induction Station.

†Major, Medical Corps, United States Army, Boston.

disqualifying allergic disease. In the *Medical and Surgical History of the War of the Rebellion*,⁴ it is reported that 4 men per thousand received medical attention for bronchial asthma while in service, and that 5 cases per ten thousand were of such severity that the men were discharged for this disability. Of the so-called "second million" drafted men examined at camps after May 1, 1918, 2.2 per thousand were rejected for asthma.⁵ *Medical and Casualty Statistics*,⁶ which gives the total figures for World War I, lists 1.9 per thousand as discharged from the Army for disability from asthma, and a total of 4.1 per thousand either rejected on induction or discharged for this condition. A national health survey,⁷ covering the years 1935-1936, estimated that 1.4 persons per thousand are annually disabled for a week or longer by asthma or hay fever. All these figures are in very close agreement.

It seems practical to consider the 1918 draft-examination figure as most closely corresponding

to the present situation. Since allergic dermatoses and other allergic states are not included, however, the true incidence of all allergic diseases is probably much higher.

tos and acute eczema, a large number of those suffering from allergic conditions are acceptable for general military service. Furthermore, Class 1-B provides for cases that are severe enough to be a liability in general military service but can at some time be of use in selected phases of military life, as they are in civil life.

Three examination periods were covered in this study (Table 1). The first, from November 17, 1940, to October 20, 1941, was the entire extent of induction-board examination of selectees who had had a previous complete physical examination by their local-board physicians. The second, from October 20, 1941, to March 15, 1942, covered pre-induction examinations in which only part of the registrants had been examined previously by the local boards and in which they were returned to their homes for from thirty to fifty days before being called to camp, a tentative rejection for special diagnostic investigation being thus allowed. The third period consisted of one month under the

TABLE 1. Results of Examinations.

PERIOD	No. OF EXAMINATIONS	No. OF REJECTIONS*	PERCENTAGES OF REJECTIONS	No. OF REJECTIONS FOR ALLERGIC CONDITIONS	PERCENTAGE OF REJECTIONS FOR ALLERGIC CONDITIONS
First (previous complete local-board examination)	18,707	3303	16	73	0.4
Second (preinduction examination, with some previously examined by local boards)	16,819	6862	40	86	0.5
Third (no previous local-board examination)	8984	3595	40	81	0.9

*Figure includes men qualified for limited military service.

to the present situation. Since allergic dermatoses and other allergic states are not included, however, the true incidence of all allergic diseases is probably much higher.

EXAMINATIONS AT BOSTON INDUCTION STATION

Examinations at this station were conducted by a team of civilian specialists. The standards followed were those prescribed in MR 1-9,⁸ which specify:

Class 1-A (qualified for general military service): May include cases of hay fever, unless severe, and of acute eczema.

Class 1-B (qualified only for limited military service): May include severe cases of hay fever; mild cases of chronic asthma that have not prevented the registrants from successfully following vocations in civil life.

Class 4 (disqualified for military service): Includes cases of chronic asthma associated with chronic bronchitis and emphysema, except as stated above, and of allergic dermatosis, if severe and not easily remediable.

Because these standards allow the acceptance of mild and moderate hay fever, mild allergic derma-

so-called "single examination" induction system, in which no man had received a complete examination by the local board. During this period, the registrant was examined and, if accepted, sent to camp on the same day.

The method of arriving at the diagnosis was reviewed in the 73 cases rejected for allergic states in the first induction period to determine the number of cases presenting diagnostic difficulties, to arrive at definite diagnostic criteria, and to establish what special investigations and findings were of most value.

Owing to the intermittent manifestations of most allergic conditions, occurring perhaps for only short intervals or at seasons other than that during which the selectee was being examined, it was impossible to use the same criteria of diagnosis that one would employ in clinical practice, in which the patient usually comes for medical examination at the time symptoms are apparent: in practice, full reliance can be placed on the history, whereas in examination by induction boards, an unsubstantiated history alone is not adequate

cause for rejection, because of the possibility of various degrees of malingering or concealment of disability.

In the 73 men rejected for allergic states, the following findings were of diagnostic value:

There were 6 cases of eczema and allergic dermatosis. The abnormal skin condition was visible at the time of examination, and a history of its relation to specific provocative irritants was obtained. (No registrant gave a history of an allergic dermatosis that was not apparent at the time of examination.)

In the 4 severe cases of hay fever, there was visible evidence of nasal allergy at time of examination, and the severity was verified by history as disabling.

There were characteristic asthmatic chest signs on routine examination in 32 of the 63 cases of bronchial asthma.

The fact that 51 per cent of the selectees with bronchial asthma had definite sibilant rales on auscultation, and that in an additional 6 per cent such signs were found later during the same day, emphasizes the value of this type of examination. Although the paroxysms of bronchial asthma are,

TABLE 2. Comparison of the Incidences of Other Abnormalities in the Allergic and Control Groups.

ABNORMALITY	ALLERGIC GROUP	CONTROL GROUP
	%	%
Chronic sinusitis	10	0
Nasal polyps	6	0
Deviated septum, deformed nose, bony septal ridge, dislocated nasal cartilage, basal spur or defective hearing	15	18
Dorsal kyphosis, severe	4	1
Neuropsychiatric conditions	20	20
Sympathetic instability	4	1
Chest expansion (average)	6 cm	6 cm.

in most cases, of short duration, one forgets that it often takes weeks for the chest signs to disappear entirely and that, in many severe cases, the chest signs are seldom absent, owing to the presence of superimposed emphysema and chronic bronchitis or bronchiectasis.

In the remaining 31 cases of bronchial asthma, which at the time of examination showed no rales and in which the diagnosis was made by the internist on an apparently unequivocal history, the special examination or findings that were of assistance in substantiating this diagnosis were: re-examination of chest eliciting characteristic musical and sibilant rales, 6 cases; documented history, 2 cases; nasal allergy, 3 cases; allergic dermatosis, 3 cases; and eosinophil count over 5 per cent, 2 cases. Although the finding of nasal allergy, or allergic dermatosis in a case of bronchial asthma is not positive verification of a suspicious history of asthma, it is evidence of an allergic state and hence may be considered at least partial sub-

stantiation. The same thing may be said, with certain reservations, of an elevated eosinophil count.

To determine the significance of other abnormalities found in the allergic group, the records were compared with a control group, made up of the 2 cases rejected following each case rejected for an allergic state (Table 2). Although the series is small (73 allergic conditions, 144 controls), certain tentative conclusions may be drawn.

Abnormalities of nose. The finding of sinusitis and nasal polyps should be considered tentatively at least as substantiating a history of an allergic condition. Although it is known that the occurrence of nasal sinusitis in bronchial asthma may be purely coincidental, the relation is so common that the error can be considered insignificant. Francis, quoted by Lord,⁹ found nasal abnormalities in 14 per cent of his 442 cases of asthma, and Rackemann¹⁰ states: "The clinical picture of asthma is not limited to the pulmonary symptoms. Lesions of the paranasal sinuses are part of it." That patients with sinusitis only rarely have asthma is, of course, well recognized. Other abnormalities of the nose and throat do not appear to be of significance in the diagnosis of allergic states.

Orthopedic abnormalities. Although more cases with marked dorsal kyphosis were recorded in the allergic group than in the control group, the number was far less than was expected. It is a fact that severe bronchial asthma in childhood produces more or less deformity of the thoracic structure. However, such defects were not sufficiently striking to be recorded by either orthopedist or internist in the rapid routine examination. Hence, a special examination of the thoracic structure may well be indicated in all cases giving a history of asthma, for although it might be expected that the chest expansion would be altered, this was not shown on routine examination.

Neuropsychiatric abnormalities. Although no quantitative and little qualitative difference could be found in the neuropsychiatric abnormalities in the two groups, the diagnosis of the allergic state was included as part of the neuropsychiatric diagnosis in 12 per cent of the 73 cases. Since the neuropsychiatric examinations were performed by a number of different examiners with very limited time at their disposal, the diagnostic criteria were not uniform. The method by which the neuropsychiatric diagnosis was made therefore requires clarification. Undoubtedly, what the psychiatrists had in mind was the psychosomatic component of allergic states. This psychiatric aspect has been referred to by others.¹⁰

X-ray findings. The chest roentgenogram was recorded as normal in all but one case of the allergic series, showing definitely that a negative finding does not rule out bronchial asthma. It was believed, however, that a greater number of positive findings of emphysema, pulmonary fibrosis, low fixed diaphragm and bronchiectasis should have been made in cases of long-standing, severe, bronchial asthma, that the routine examination was not giving sufficient information and that additional roentgenographic study was advisable. The 4-by-5-inch stereoscopic photoroentgenogram without grid in routine use gives an exaggeration of the lung markings at the bases that has to be minimized in interpretation. It may prove advisable to take 14-by-17-inch films in men with a history of long duration and severity.

Verification and detailed history. It is hard to conceive of a registrant with bronchial asthma of sufficient severity to warrant rejection who has not sought medical attention at some time; therefore, when such verification is easily available, it is often the most efficient method of substantiating the diagnosis. The statement from a reputable physician or clinic of having observed the patient in attacks of asthma was considered adequate to substantiate the history.

Obtaining a detailed allergic history, including the descriptions of attacks and all manifestations of allergy, is far different from merely hearing the registrant's statement that he has bronchial asthma. It is difficult to give such a history without an intimate subjective knowledge of the disease. For this reason, when other evidence was not easily available, the detailed history was relied on in a few cases; however, later study proved that the greatest advantage of the complete history was to determine the exact nature of the case so that a search could be made for whatever manifestations might be expected.

Eosinophil count. Although the eosinophil count is elevated in some parasitic conditions, in this locality they are sufficiently rare so that a count of 4 per cent or over is regarded as substantiating the allergic state, provided that no history of these parasitic and certain other conditions is obtained.¹¹ It has been shown by Baagöe¹² that the count may remain elevated one month after an attack—a fact that makes it exceedingly useful in diagnosis, especially in registrants with a history of an asthmatic attack within a few weeks but with no objective evidence of the disease.

Eosinophil counts were made in a small series of suspected cases and nonselected controls. In the control series (24 cases), no eosinophil count was over 3 per cent. The counts in 6 cases suspected of allergy and proved negative were less than 2 per cent. When eosinophil counts were made in the remaining 18 patients, disqualified because of allergic states, the counts were over 5 per cent in 5 (28 per cent).

First Series

Four selectees out of the 18,707 examined in the first period at the Boston Induction Station were discharged from camp on Certificate of Disability Discharge for bronchial asthma. This is not the total figure, since it does not include those examined in this and discharged in other corps areas, but it probably comprises roughly 50 per cent of the total. The records of these cases were reviewed. In none was there any history of allergy or respiratory abnormality. In only one were there findings that might have aided in a diagnosis of allergy. In that case, there was dorsal kyphosis, poor posture and a chest expansion of only 4 cm. This suggests that more specific questions should be asked to elicit a history of allergy and that more attention should be given to abnormal thoracic structures.

Diagnostic errors were apparently less frequent than might be expected in such rapid routine examinations. A few selectees who were rejected for bronchial asthma on the finding of sibilant and musical rales and a doubtful history later returned and were accepted. With the great num-

ber of acute respiratory conditions seen at some periods, such an error seems unavoidable but would be minimized by adherence to the present criteria and by following Paragraph 49b of MR 1-9, which states that Class 1-A may include cases of "acute bronchitis, providing acceptance is temporarily deferred until a final examination shows recovery without disqualifying sequelae." When this procedure is followed, roughly half return completely recovered; the rest continue to have chest signs over a period of months and are rejected for chronic bronchitis or bronchial asthma.

Rejection was considered in a few cases in which a verified history of childhood asthma was obtained, but with no symptoms in the previous five years. Such a history is inadequate proof of bronchial asthma, and is of such doubtful significance in adult life that disqualification appears unwarranted. In 2 cases in which a clinical diagnosis of bronchial asthma was made, the x-ray findings were those of moderately advanced pulmonary tuberculosis. Several selectees, believing that they had asthma, based on an isolated attack of "wheezing" several years previously for which they had sought medical attention, had been skin tested and instructed to avoid certain allergens. Such isolated attacks do not warrant a diagnosis of bronchial asthma.

No frank case of malingering of feigned allergy was discovered in the examinations of the first period, although several were suspected in which the allergy was proved; several cases were found, however, in the last examination period. Negative malingering was commoner. Three selectees, ignorant of the seriousness of the offense, concealed from the examiner the fact that they had had severe bronchial asthma when asked general questions concerning their past illnesses. Three selectees answered in the affirmative to all questions regarding allergic symptoms and were found to be nonallergic; all, however, were mentally deficient.

Second Series

Little information was gained in the second pre-induction examination period, although 86 men were rejected for allergic conditions. This lack of information was largely due to the fact that doubtful cases could be classed as "tentative rejections" and requests made for such examinations and verification of history as were necessary for diagnosis. This removed the pressure of having to make a definite decision on the day of examination, and thereby eliminated the stimulus to investigate diagnostic criteria. Theoretically, this method should be extremely accurate because more study can be made of the cases. The results were illuminating, because none of the cases were

returned with any information that could not have been obtained on the day of examination.

In this period, a detailed study was made of the first 4000 selectees. Of this number, 18 were disqualified for allergic states; all were verified by history. Musical and sibilant rales were heard in 11 cases; 1 man had dorsal kyphosis and 3 had chronic sinusitis and nasal polypi. Neuropsychiatric substantiation was obtained in 1 case, and increased bronchial markings on x-ray study in 1 case. Seven tentative rejections (28 per cent) were made, with requests for verification of history, eosinophil counts and skin testing.

Third Period

With the knowledge gained in the first two periods, a study was made to determine the efficiency of the examinations in the first 68 cases in this period in which the registrant gave a history of bronchial asthma (Table 3). Of these, 58 were

TABLE 3. Pertinent Findings in 58 Selectees Disqualified for Bronchial Asthma.

FINDING	No. of Cases	Per Cent
Documentary history	28	49
Eczema	6	10
Sinusitis or verified history of sinusitis	—	12
Sibilant or musical rales on auscultation (either on examination or re-examination)	45	78
Thoracic structural abnormalities (dorsal kyphosis or increased anteroposterior dimensions on examination or re-examination)	20	35
X-ray abnormalities	6	10
Emphysema	2	
Pulmonary fibrosis	2	
Fixed low diaphragm	1	
Bronchiectasis	1	
Neuropsychiatric conditions (psychoneurosis with allergy or psychosomatic syndrome)	6	10

verified and the registrants rejected. Eight men were accepted, 3 because the condition had not been present for five years, and 5 because of the absence of any evidence of asthma at the time attacks were claimed or because of documentary evidence that the asthma did not exist. Two cases were proved to be recurrent acute anxiety states, and the men were consequently rejected.

In all cases, a detailed history elicited an intimate subjective knowledge of the disease, and one or several of these pertinent findings were present. The findings in this series confirmed the conclusions arrived at previously and also showed that more special attention to chest roentgenograms and the thoracic structure demonstrated more significant abnormalities than had been seen on previous routine examinations. It could not be decided whether the discovery of malingering in 6 cases, in the last induction period, demon-

strated error in the previous examinations or a general increase in attempted evasion of military service.

DISCUSSION

The diagnosis of allergic states by examining boards resolves itself into a detailed study of each case, presupposing an intimate knowledge on the part of the examiner of the many manifestations of these conditions, and the residua apparent during the intermissions between acute episodes.

Every registrant is asked whether he has ever had asthma, bronchitis or hay fever. His history form is inspected to see if he has mentioned these or other related conditions. If a history of bronchial asthma is elicited, especially careful attention is given to auscultation of the chest. If there has been an attack within three weeks, fleeting musical rales may frequently be expected. Many men with the history of an old severe asthma, but with no attacks within a few years, are found to have chronic asthmatic bronchitis and emphysema at all times.

The complete allergic history is carefully taken, with special attention to determine from the duration, frequency, severity and precipitating factors just what condition would be expected at the time of examination. In all cases of asthma, and especially if the story is one of a severe asthma in childhood, the chest contour must be carefully inspected for increased dorsal kyphosis, barrel chest and increased anteroposterior diameter. A note should be sent to the radiologist to give the chest film special attention and to take a 14-by-17-inch film, if necessary. In men with a history of attacks within two months, an eosinophil count should be requested if the diagnosis is not otherwise verified. The history should include a detailed account of all previous medical attention. This often points out the severity and disabling nature of the condition and also gives the sources from which a documented history may be obtained.

In all cases, the skin must be carefully inspected, especially the face, ears and elbows, for eczema, which is often present between asthmatic attacks. The skin should be stroked to test for dermatographia. The results of the nose and throat examination should be noted, and the finding of nasal allergy, sinusitis or nasal polypi should be considered significant. All questions of purulent nasal discharge and chronic rhinitis should be solved by x-ray examination of the nasal sinuses. The results of the neuropsychiatric examination are studied, and the inclusion of the diagnosis of allergy as part of the neuropsychiatric diagnosis is considered substantial verification.

CONCLUSIONS

At the Boston Recruiting and Induction Station, 220 registrants out of 45,000 examined, or 0.5 per cent, were disqualified for general military service because of severe allergic states. This number compares closely with the known prevalence of these conditions in the general population of this age group.

The errors of the examination were considered. A known 4, and an estimated 8, selectees from the first 18,707 examined were discharged from camp for bronchial asthma within six months. In none of the 4 cases was a history of the condition obtained.

It is believed that even men with mild cases of asthma should be disqualified for general military service because of the probability of frequent illness, serious residua after subjection to chemical warfare, and greater risk of compensation.

Contrary to what might be expected, no information was gained in the preinduction period by the making of tentative rejections for further information and examination that could not have been gained on the day of examination.

It was found that an adequate diagnosis could be made from routine examination in only 60 per cent of the cases. This indicated the need for investigating what findings and examinations were of most value in substantiating the diagnosis; these include the presence of nasal sinusitis or nasal polypi, examination of the thoracic structure for dorsal kyphosis and an increased anteroposterior

diameter, positive neuropsychiatric findings, positive chest findings on auscultation, a documented or verified allergic history and a high eosinophil count. The roentgenogram was of assistance in only from 2 to 10 per cent of cases, depending on whether it was a routine or special examination; hence, a normal chest film in no way eliminated bronchial asthma.

With the assistance of these findings, and by setting not too stringent criteria for diagnosis, an examining board will find little trouble in the diagnosis of allergic states.

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ASCORBIC ACID DEFICIENCY ASSOCIATED WITH GASTRIC LESIONS*

CHARLES C LUND, M.D.†

BOSTON

IN recent publications, Lund, Crandon and Dill^{1, 2} have presented data concerning the relation of ascorbic acid to the healing of wounds. These data were secured by a study of patients whose wounds failed to heal. From these studies, conservative conclusions were drawn concerning the relative importance of ascorbic acid and various other factors (technical and chemical) as causes of failure of healing. The authors believed that, in the series studied, ascorbic acid deficiency caused fewer failures of healing than technical factors did. As a result of a similar study of cases with disrupted wounds, Hartzell, Winfield and Irwin³ have taken the same conservative position, placing ascorbic acid deficiency among other factors as a possible cause of delayed or poor healing. Holman,⁴ who studied routine surgical admissions, found that many patients had low blood plasma levels of ascorbic acid, but he did not state that disruption occurred in any of the particular cases studied. Bartlett, Jones and Ryan⁵ showed that, in addition to low plasma ascorbic acid levels, many patients had abnormally low clearance curves in the plasma and low excretion in the urine after the administration of test doses. A recent paper by the same authors⁷ presents experiments in which the tensile strength of healing tissues of animals and men were tested and the ascorbic acid content of the healing tissues determined. These studies show that low plasma levels are associated with low levels in the healing tissues, and that this, in turn, is associated with delayed healing. Wolfer and Hoebel⁶ studied several cases of gastrointestinal carcinoma and other conditions. One patient without treatment was found to have a very low level of plasma ascorbic acid after evisceration. Other patients with low levels were treated, and no evisceration occurred. Ludden, Flexner and Wright⁹ found, in 23 cases with gastric lesions, that only 1 patient had a normal ascorbic acid reserve, and 1 had frank scurvy. They report that 7 gm of ascorbic acid was necessary to saturate the latter patient. Hunt¹⁰ studied the problem of vitamin C and healing in

both experimental animals and man. A particularly interesting part of the study was that done on 28 patients who came to autopsy shortly after surgical operation. He found that in 8 there was microscopic evidence of failure of deposition of collagen in the wounds; 5 had disruption of the abdominal wounds, and 3 had leakage of anastomotic suture lines.

The present communication is concerned with data on a group of patients with gastric lesions. These cases are of especial interest because ascorbic acid deficiency is very common among them, not because of any direct metabolic effect of the disease, but purely because of deficient dietary intake of the vitamin. In this study, an attempt was made to estimate as closely as possible the tissue reserves of the vitamin. These reserves are what is probably important in the healing of the wound rather than the output in the urine or the amount in the blood plasma, both of which may be affected by changes much more rapidly than the reserves are. It was hoped that by focusing attention on the reserves a better understanding of the problem might be secured.

METHODS

Dietary history. Analysis of the patient's diet, one of the many ways of studying the ascorbic acid status, is available to any physician and needs no laboratory tests. Without such tests, however, it can give only part of the picture, but the part given is so important that even when laboratory tests are available it must not be omitted. For some time, there have been available complete tables giving fairly accurate analyses of the vitamin C content of all usual American foodstuffs.¹¹ By taking a dietary history and calculating from the tables, one may make a fair estimate of the vitamin C intake over as long a period as the history is reliable. It must be realized that studies for a day or two are of little value. What is needed are averages over long periods. Ralli et al.¹² have shown that, when diets are changed, the blood plasma level changes with them, and rather promptly becomes adjusted to the new level of intake, except that no increase in intake can cause a further rise in the level after the tissues and blood become saturated. From the length of time shown by Crandon, Lund and Dill² to be necessary for the de-

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†From the Fifth Surgical Service, Boston City Hospital and the Department of Surgery, Harvard Medical School.

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†Assistant professor of surgery, Harvard Medical School, visiting surgeon in Boston City Hospital.

velopment of scurvy in a healthy man, it is certain that the adjustment of the reserves to changes in the diet is much slower than the adjustment of the blood plasma level. In giving consideration to the dietary calculations, one must take account of the possible interference with intake caused by vomiting and the interference with absorption caused by diarrhea. There is also evidence that the needs of the system are increased in conditions causing increased metabolism, such as fever and hyperthyroidism. In this study, the dietary calculations were based on the average intake for one month prior to the first blood test. It is realized that a longer period of consideration would be helpful if there were marked variations in intake prior to a month, but it was found to be impractical to evaluate data that went back farther than this.

Blood plasma studies. If the patient is on a definite daily intake of vitamin C and is in a constant state so far as absorption and metabolism are concerned, a single plasma determination will give a fair index of the degree of saturation. Unfortunately, however, a very short period of reduced intake or increased utilization will affect the plasma level much more than it will affect the tissue reserves. A single determination showing a saturation level (about 1.0 mg. per 100 cc.) is all that is needed to prove that a patient's reserves are saturated, but a determination of 0.00 may be found in a person who has a 75 per cent reserve, and the same value may be found in a patient with scurvy.² A low value with high reserve may be due to illness, operation,¹³ starvation or vitamin C deprivation of only two or three weeks' duration.

When a low value has been found, one can, however, determine how low the depletion in reserves is by replacing the vitamins and measuring the amount and time needed to achieve saturation. Two general types of saturation tests have been used in the past. In one, hourly determinations of the plasma level are made after a test dose of, usually, 1 gm.¹⁴ The shape of the resulting curve indicates the degree of depletion. The other, and the one used in this study, is to give daily doses, usually 1 gm. each, and determine the level on the following mornings.¹⁵ A true case of scurvy will need four to six doses before the patient shows a normal level in the morning.² If one finds, however, a saturation level on the second morning, one can be sure that the patient had half or more of his normal tissue reserves before the test began.

Vitamin C in white blood cells. Butler and Cushman¹⁶ showed that the normal person with saturated vitamin C reserves has a level of 30 to 40 mg. per 100 gm. in the white blood cells. They,

and Crandon, Lund and Dill,² have shown that this level drops off much more slowly on deprivation than the level in the plasma does. However, even this value does not always have a direct relation to the reserves, since the level reaches zero some time before the symptoms of scurvy appear. Values for the white cells were included in the data on a few of the cases in this paper.

Estimation of reserves. The estimate of ascorbic acid reserves is made on the basis of all the data available in each case. In all cases except Case 1, there was evidence of at least two of the following kinds: history, simple plasma determination, simple white-cell determination, and determination of plasma or white cells after test doses. When diet or simple plasma or white-cell determinations were the only data available, the reserve was taken at the level suggested by the one that indicated the position nearest to its normal. If determinations were made following test doses or treatments, the results of these tests were made the basis of the estimate, as follows: if the plasma value was found to be 1.0 mg. per 100 cc. the morning after a dose of 1.0 gm. of ascorbic acid, the value was entered as 75 per cent because, no matter what the original plasma determination showed, the reserve could not have been appreciably lower than this; on the other hand, if the plasma determination was still 0.0 mg. after three daily doses of 1.0 gm., the reserve was entered as 0. Other results were entered at intermediate levels depending on the best estimate of the reserve.

DATA

Table 1 presents data on 18 patients with non-radical, elective operations for ulcers of the stomach and duodenum. The indications for operation were intractability to medical treatment, obstruction or bleeding or some combination of these. The first column in the table shows the usual dietary intake during the month prior to study. It should be noted that most of the cases had very low intakes. The second and third columns show the pretreatment plasma and white-cell values. The fourth shows the estimate of the reserves. In some cases, particularly Cases 3 and 9, higher values are given than can be directly estimated either from the diet or the plasma value. The estimate in such cases was made on the basis of a later saturation test that proved that neither the history nor the plasma value indicated the true situation. In general, whatever evidence indicated the higher value for the reserve was considered to be most nearly correct for a particular case. The fifth column indicates the amount of ascorbic acid given either by mouth or intrave-

nously prior to operation or up to four days after operation. The sixth shows the reserve established by the addition of this treatment to the prior reserve. The seventh column gives the type of oper-

long time and was in a particularly depleted condition in every way. He had so little vitamin C reserve that he was very close to scurvy. Although this deficiency was taken care of, it is possible that

TABLE 1. *Data on Ascorbic Acid Reserves before and during Healing in Nonradical Operations for Gastric and Duodenal Ulcers.*

CASE No.	CONDITION BEFORE TREATMENT				PRELIMINARY ASORBIC ACID RESERVE		TYPE OF OPERATION	SUBSEQUENT ASORBIC ACID TREATMENT	RESULT OF OPERATION
	ASORBIC ACID IN DIET	PLASMA ASORBIC ACID	WHITE-CELL ASORBIC ACID	ASORBIC ACID RESERVE	PRE-TREATMENT	RESERVE AFTER PRELIMINARY TREATMENT			
	mg / day	mg / 100 cc.	mg / 100 gm.	%	gm	%		gm	
1	1	0.15	—	15	0.0	10	Posterior gastroenterostomy	0.0	Cerebral hemorrhage, death.
2	100	0.74	—	100	0.0	100	Posterior gastroenterostomy	1.2	Recovery
3	2	0.00	—	20	2.4	40	Posterior gastroenterostomy	0.0	Recovery
4	5	0.13	—	15	1.6	40	Posterior gastroenterostomy	0.0	Recovery
5	40	0.62	—	60	0.0	60	Pyloroplasty	0.0	Recovery
6	5	0.11	—	10	0.6	25	Posterior gastroenterostomy	7.0	Recovery
7	10	0.10	—	10	0.0	10	Posterior gastroenterostomy	0.0	Recovery
8*	10	0.10	—	20	5.6	100	Jejunostomy	7.9	Recovery
9†	25	0.21	—	40	0.0	40	Posterior gastroenterostomy	0.0	Recovery
10	15	0.11	—	15	0.0	15	Excision of gastric ulcer	0.0	Recovery
11	5	0.30	—	30	4.0	100	Posterior gastroenterostomy	3.0	Recovery
12	5	0.00	3.0	10	0.0	10	Posterior gastroenterostomy	0.0	Disruption, recovery
13	5	0.00	6.5	30	1.0	50	Posterior gastroenterostomy	4.0	Recovery
14	5	0.05	7.8	40	2.0	100	Posterior gastroenterostomy	0.0	Recovery
15‡	10	0.05	6.0	25	0.0	25	Posterior gastroenterostomy	4.0	Recovery
16§	15	0.01	4.2	25	4.0	100	Jejunostomy	0.0	Recovery
17	1	0.00	1.3	5	4.0	80	Jejunostomy	0.0	Peritonitis, death
18	5	0.02	1.4	5	5.0	100	Posterior gastroenterostomy	0.0	Recovery

*Same as Case 7, Table 3

†Same as Case 8, Table 3.

‡Same as Case 13, Table 2

§Same as Case 12, Table 3

ation, and the eighth shows the amount of ascorbic acid given subsequent to healing. The last column lists the result of the operation. The patient in Case 1 died the day after operation with symptoms suggestive of a cerebral hemorrhage. It is

other deficiencies that were not corrected may have contributed to his death.

Table 2 presents similar data on a group of 18 cases with ruptured gastric or duodenal ulcer. Necessarily, these patients were studied after operation.

TABLE 2. *Data on Postoperative Ascorbic Acid Reserves in Cases with Suture of a Ruptured Gastric or Duodenal Ulcer.*

CASE No.	POST-OPERATIVE DAY OF STUDY	CONDITION AT TIME OF STUDY			PREVIOUS ASORBIC ACID TREATMENT	ASORBIC ACID RESERVE	SUBSEQUENT ASORBIC ACID TREATMENT	RESULT OF OPERATION
		ASORBIC ACID IN DIET	PLASMA ASORBIC ACID	WHITE-CELL ASORBIC ACID				
		mg / day	mg / 100 cc.	mg / 100 gm.	gm	%	gm	
1	1	25	0.30	—	0.0	50	0.0	Recovery
2	1	150	0.17	—	0.0	100	0.0	Recovery
3	10	—	0.12	—	0.0	10	2.0	Disruption death
4	1	8	0.10	—	0.0	10	0.0	Duodenal fistula, death
5	1	7	0.10	—	0.0	10	0.0	Recovery
6	49	50	0.10	—	0.0	50	4.0	Flyphlebitis, death
7	1	55	0.28	—	0.0	30	7.0	Recovery
8	14	—	0.19	—	0.0	30	5.0	Dehiscence recovery
9	21	45	0.12	—	0.0	50	0.6	Subphrenic abscess recovery
10	15	10	0.10	—	0.0	30	4.0	Peritonitis, death
11	10	9	0.10	—	0.0	50	11.1	Disruption recovery
12	10	4	0.10	—	0.0	50	9.0	Dehiscence, death
13*	11	10	0.05	6.0	0.5	25	4.0	Recovery
14	1	5	0.03	13.0	4.0	100	0.0	Recovery
15	1	10	0.07	4.0	0.0	20	0.0	Recovery

*Same as Case 15, Table 1.

barely possible that the very low level of vitamin C may have contributed to his death. The patient in Case 12, which has been previously reported,¹ had a disruption due largely to scurvy. Case 17 was that of a man who had been vomiting for a

In a large number, including all but one that had complications, they were studied after complications arose. For this reason, the series is not a fair sample of the work in the hospital, and the high mortality of these cases is much higher than

the hospital average. The very low values for plasma ascorbic acid must be viewed in the light of the time the blood was taken. Both the operations¹³ and the complications probably depressed these levels.

Table 3 shows data similarly arranged for 15 cases having major operations for the removal of benign gastric and duodenal lesions. It will be seen that more of these cases had fairly good vitamin C reserves prior to the immediate preoperative period and that many of the deficient cases were

tured gastric ulcer are not included because post-operative depressions of the value make direct comparison with the other cases impossible). Levels of less than 0.10 mg. were found ten times in the same number of operations. White-cell values were available in only a few of the cases. None showed a saturated level (30 mg. per 100 gm.), and 7 out of 13 patients gave evidence of a very depleted, but not necessarily scorbutic, state.

It is also clear that very few of the cases showed evidence of saturation before treatment. In fact,

TABLE 3. *Data on Ascorbic Acid Reserves before Treatment and during Healing in Radical Operations for Gastric or Duodenal Ulcer.*

CASE No	CONDITION BEFORE TREATMENT				PRELIMINARY ASCORBIC ACID TREATMENT	ASCORBIC ACID RESERVE AFTER PRELIMINARY TREATMENT	OPERATION	SUBSEQUENT ASCORBIC ACID TREATMENT	RESULT OF OPERATION
	ASCOR- BIC	PLAS- MA	WHITE CELL	ASCOR- PIC					
	ACID	ASCOR- BIC	ASCOR- BIC	ACID					
	IN DIET	ACID	ACID	RI- SERVE					
	mg / day	mg / 100 cc	mg / 100 gm	%	gm	%		gm	
1*†	14	0.15	—	15	0.0	15	Right colectomy	0.0	Pneumonia, recovery
2	—	0.34	—	35	0.0	35	Partial gastrectomy	0.0	Pneumonia, recovery
3	—	0.38	—	40	0.0	40	Partial gastrectomy	2.1	Recovery
4	15	0.20	—	20	1.0	40	Partial gastrectomy	0.0	Leak, death
5*	60	0.60	—	60	0.0	70	Partial gastrectomy	2.0	Pneumonia, recovery
6	50	0.83	—	60	3.0	100	Partial gastrectomy	0.0	Peritonitis, death
7‡	10	0.50	—	100	14.5	100	Partial gastrectomy	0.0	Leak, death
8§	25	0.10	—	25	0.0	25	Partial gastrectomy	0.0	Recovery
9	60	—	—	60	6.4	100	Partial gas rectomy	5.5	Recovery
10	—	0.10	—	30	0.0	31	Partial gastrectomy	2.0	Recovery
11*	15	—	—	20	0.7	40	Partial gastrectomy	0.0	Pulmonary abscess recovery
12*	15	0.00	4.2	25	7.4	100	Partial gastrectomy	1.6	Recovery
13	10	0.14	14.0	70	2.0	100	Partial gastrectomy	4.0	Disruption, recovery.
14	5	0.01	1.0	5	2.0	50	Partial gastrectomy	2.0	Recovery
15*	45	—	—	50	1.5	90	Partial gastrectomy	0.0	Disruption, recovery

*Cases 1 and 5 are the same patient, who had a two stage resection of a gastrojejunocolic fistula

†Cases studied postoperatively.

‡Same as Case 8, Table 1

§Same as Case 9, Table 1

†Same as Case 16, Table 1

treated with ascorbic acid either just before or just after the operation. It should be noticed that 3 patients were studied only after complications had set in, ten, eight and ten days, respectively, after operation.

DISCUSSION

Status of Ascorbic Acid Reserves Before Treatment

A total of forty-eight gastric operations were done on 43 patients. If one takes a conservative position in regard to diet by considering that a daily intake of 50 mg. should maintain a sufficient reserve for all purposes, the histories indicated that in only 7 of 43 patients was this level recorded. In 16 of 43 cases, the record showed a daily intake of less than 10 mg. However, in 5 of these, the history must have erred because other data showed higher reserves than such an intake would be likely to maintain. If one considers that a plasma level of 0.60 mg. per 100 cc. shows a reasonably saturated condition, it is evident that this level was found in only 4 of 31 cases (the cases with a rup-

tured gastric ulcer are not included because post-operative depressions of the value make direct comparison with the other cases impossible). Eight cases were rated at 10 per cent or less.

Status of Reserves at Time of Healing

Early in the study, it was found that many cases with very low plasma levels healed properly in every way, so that no effort was made to have the condition corrected in all cases at once. Therefore, many cases that probably should have been treated with ascorbic acid were not. It will be seen from the "preliminary treatment" and the "reserves at time of study" columns that some cases were not treated, but that many were. The latter is particularly true in the cases with radical operations. It is also seen that, in many cases, treatment was started or continued after the primary healing period was over. This was especially so in the cases of ruptured ulcer with complications.

Importance of Reserves at Time of Healing

It is impossible to visualize systematic differences of results in accordance with differences in the

ascorbic acid reserves by inspection of the three tables already presented. However, Table 4 summarizes some of these data in a form in which they can be visualized. Everything is left out except the vitamin reserves during the healing period and the results. The cases are divided into three groups: those with reserves of 0 to 20 per cent, 25 to 50 per

It is well realized that it is dangerous to claim that diverse postoperative complications are in any way due to vitamin C deficiency. Lund and Crandon³ have already presented data showing lack of correlation between vitamin C levels and the development of postoperative pneumonia. Others, however, especially Hunt,¹⁰ have believed that

TABLE 4 Complications and Deaths following Operations for Gastric or Duodenal Ulcer in Relation to Ascorbic Acid Reserves at the Time of Healing

SOURCE	RESERVES AT TIME OF HEALING	TOTAL NO. OF CASES	CASES WITH ONLY COMPLICATIONS	CASES WITH NONFATAL COMPLICATIONS	DEATHS	PERCENTAGE OF COMPLICATIONS AND DEATHS	PERCENTAGE OF DEATHS
Table 1	0-20 per cent	4	2	1	1	50	25
	25-50 per cent	6	6	0	0	0	0
	55 per cent or over	8	7	0	1	13	13
	Total or average	18	15	1	2	6	11
Table 2	0-20 per cent	4	2	0	2	50	50
	25-50 per cent	0	3	3	3	67	33
	55 per cent or over	2	2	0	0	0	0
	Total or average	15	7	3	5	53	33
Tables 1 and 2	0-20 per cent	8	4	1	3	50	38
	25-50 per cent	15	9	3	3	40	20
	55 per cent or over	10	9	0	1	10	10
	Total or average	33	22	4	7	33	21
Table 3	0-20 per cent	1	0	1	0	100	0
	25-50 per cent	7	4	2	1	43	14
	50 per cent or over	7	2	3	2	63	29
	Total or average	15	6	6	3	40	20
Tables 1, 2 and 3	0-20 per cent	9	4	2	3	67	33
	25-50 per cent	22	13	5	4	41	18
	50 per cent or over	1	11	3	3	35	18
	Total or average	48	28	10	10	42	21

cent and 55 per cent or over. Results are also divided into three groups: recovery without complications, recovery after complications and death. The complications are all grouped together.

The most significant data in this table are found by comparison of the results (percentage of complications and deaths) derived from Tables 1 and 2 with the corresponding figures from Table 3. The number of cases is small, and conclusions derived from such a small series of cases must be guarded. There is, however, an apparent correlation between complications and deaths and low vitamin C reserves in the cases presented in Tables 1 and 2, but none in Table 3. What does this mean? Only a suggestion can be made. Such operations as closure of a ruptured ulcer and gastroenterostomy are so simple that technical errors are very unlikely. Therefore, if there are marked variations in the medical aspects of the cases, these variations rather than technical ones are likeliest to determine complications. On the other hand, the technical difficulties encountered in the major gastric resections were so frequent and so great that the variations, if any, resulting from the medical aspects of the cases did not show up.

many cases of postoperative peritonitis are due to failure of wound healing. It will be seen that all the complications of the cases listed in Tables 1 and 2 comprised complete disruption of the wound or peritonitis, which, in every case, could have resulted from failure of the gastrointestinal suture line to heal, except the complication in Case 1, Table 1. The data suggest that low vitamin C was a major complication of the remainder of the cases.

Vitamin Treatment of Surgical Cases

The vitamin treatment, if any, given these patients was usually limited to ascorbic acid, but in a few cases, one or more of the following vitamins were given: vitamin A, vitamin D, thiamine and nicotinic acid. All the cases of gastric resection had transfusions of at least 500 cc of whole blood, and a few of the others received similar treatment.

The fact that, in many of these cases, no benefit can be shown to have resulted from vitamin treatment does not indicate that it was useless. The failure to demonstrate results may mean only that the treatment was "too little and too late."

must not forget that most of the cases showing more than 50 per cent depletion below saturation of ascorbic acid may have had more serious, but unrecognized, deficiencies of other vitamins, minerals or even of types of protein. It is more than possible that some of these other deficiencies are more significant than that of ascorbic acid. As methods of study become available, they should be applied to such cases. In the meantime, the position taken by Holman⁵ of giving large doses of all vitamins to all cases undergoing major surgery may be a wise one. It should also be remembered that, when vitamins are ordered, they should be given parenterally if there is any chance of poor absorption.

CONCLUSIONS

Very few of 45 patients who underwent operations for gastric lesions had a normal ascorbic acid intake, plasma level, white-cell level or reserve.

A few cases had such low reserves that they must have been very close to scurvy.

The greatest number of cases had from 20 to 50 per cent of normal reserves.

When nonradical operations were performed, more complications and deaths occurred in the patients with low reserves than in those with high reserves.

No more complications or deaths occurred in patients with low ascorbic acid reserves after radical gastric operations.

It is suggested that more and better vitamin treatment is indicated in cases coming to gastric surgery.

319 Longwood Avenue

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PRACTICAL PSYCHIATRY WITH ADOLESCENTS

III. Technic of Psychotherapy for the General Practitioner

DANIEL J. SULLIVAN, M.D.,* AND OTTO BILLIG, M.D.†

ASHEVILLE, NORTH CAROLINA

IN the first paper¹ of this series, a general discussion of the problems of the adolescent outlined various difficulties of adjustment met by the adolescent as he advances from late childhood to early adulthood, and the opportunity for help from the family physician was stressed. In the second paper,² a practical method for psychiatric examination was detailed, the minimal but necessary technical knowledge being explained. In this concluding paper, methods of psychotherapy and illustrative case histories are presented, so that the essentials for a mental-hygiene approach to these patients can be readily utilized.

The older child and the adolescent do not need excessive care in handling the many problems of adolescence; they can do most of the adjusting themselves. What they do need for the most part is understanding rather than actual help and, particularly, encouragement to seek and maintain an increasing independence of family. How unsuccessful an adolescent is in meeting his problems is expressed by his conduct, which is an exaggeration of behavior patterns formed in early childhood.

Personality reactions underlying adolescent behavior result in three general types: the paranoid, who believes that others always "pick" on him, resents correction, and is constantly dissatisfied; the introvert (schizoid), a shy, seclusive person who retires into daydreaming and fantasy formation; and the offensive patient, who is defiant, antisocial and the leader of rebellious groups, and who basically has a great deal in common with the paranoid. These types occur mildly at some time or other in all adolescents, but are pathologic when any one becomes marked and fixed in a certain person.

The commonest feeling resulting from unsuccessful adjustment is inferiority. Ordinarily, such feelings result from one or more of the following: an oversolicitous mother who prevents the child from "growing up" and hence makes him unable to hold his own in competition; a stern father who sets standards too high for the child to reach with any personal satisfaction of measuring up;

physical defects magnified by overzealous parents and others; and relative mental dullness in a child who is made to compete with children of higher intelligence. Feelings of inferiority usually develop with adequate bases, whereas a so-called "inferiority complex" is an exaggerated degree of such feeling.

As described in the second paper of this series, the important investigative and diagnostic points may be enumerated as follows: neurotic traits; daydreaming and fantasy life; personal ambition; loves and attachments; secret fears and uncertainties; psychic trauma; sexual knowledge or misbeliefs, experiences and fears; intrafamily relations; and any symptoms of a psychosis. After determining the presence, quality and quantity of these traits, along with any other evidences of maladjustment, one is in a position to outline a plan of treatment.

METHODS OF TREATMENT

Explanation, reassurance and desensitization are the essential methods of direct psychotherapy so far as the general practitioner's training and time permit. This, of course, presupposes that he has gained the confidence of the adolescent and can act as a sort of father-confessor to him. The combination of the traditional "family physician" and modernization by training in psychology and psychotherapy is the ideal sought. One cannot tell these adolescents to "buck up," "forget it" or "cut out the kid stuff"; one cannot threaten them with reform school or insanity, or laugh at their often ridiculous beliefs concerning sex, methods of physical culture to become a strong man, fantasies of achieving renown and so forth. Instead, one must permit them to unburden completely, encouraged by gentle questioning and fortified by the absence of any disciplinary or condemnatory atmosphere. Later, the encouraging of self-discipline and of the recognition and acceptance of personal responsibility can be gradually inculcated.

When the whole story, or most of it, has been obtained from the patient, and the available outside history has been evaluated, the process of desensitization should be the next step. All experiences and ideas that have caused the adolescent acute shame, embarrassment, anxiety or fear should be calmly and completely explained; the patient

*Assistant director, Highland Hospital, and medical director, Asheville Community Mental Hygiene Clinic, Asheville, North Carolina; instructor in psychiatry, Duke University, Durham, North Carolina.

†Associate in psychiatry, Highland Hospital, Asheville, North Carolina; instructor in psychiatry, Duke University, Durham, North Carolina.

should be particularly impressed with the fact that he is suffering the emotional "growing pains" subsequent to trying to discover himself as he rapidly matures. Pointing out evidences of the physical changes of puberty as coincidental physical "growing pains," the analogy being based on the fundamental unity of mind and body, is a good way to combine answers to both emotional and physical problems.

Explanation, reassurance and desensitization are direct methods of psychotherapy, but the indirect methods, such as a daily schedule of activities to fill up the adolescent's day, a modification of parental attitudes, and major or minor changes in school environment, are often as helpful.

The *daily schedule* should include school hours followed by an interval spent in a part-time job, athletics or group hobbies; evenings should be reserved for study and individual hobbies. Friday and Saturday evenings should be set aside for motion pictures, dances and parties, Saturdays for part-time jobs and athletics or other outdoor activities (boy scouts, hikes, nature clubs and so forth) and Sundays for church attendance and outdoor activities or quiet social groups at home. Idleness and loafing rather quickly foster restlessness and dissatisfaction, loss of interest and initiative toward the future, and even frank delinquency.

Hobbies should be of indoor and outdoor, and of individual and group types. Indoor hobbies have the advantage of year-round availability, whereas outdoor hobbies are usually seasonal or at least partially dependent on the weather. Solitary hobbies are useful for the adolescent who is particularly restless and flighty, since they promote perseverance and concentration. Group hobbies afford social contacts that are primarily of common intellectual interest, but adequate overflow into less impersonal relations readily occurs. This type of hobby is well worth fostering in the shy adolescent who feels woefully inadequate but often can be drawn out; in others, the intellectual liaison is established, and then, gradually, the aura of friendship appears.

The adolescent should be encouraged into actively investigating the subject of hobbies; he should be given some good references³⁻⁵ and should be encouraged to patronize the local library, Y. M. C. A., Boy Scouts and organized hobby groups. The following are more specific suggestions of hobbies:

Indoor:

Collecting — stamps, coins, autographs, minerals, semi-precious stones, Indian relics, curios of all types, antiques, art works and books.

Plants and animals (raising and training, or just pets).
Manual arts — woodworking, metal working, model making, leather working and weaving.

Fine arts — drawing, painting, engraving, sculpturing, music, literature and photography.

Entertainment — magic and sleight-of-hand, impersonations and fortune telling.

Sciences — astronomy, radio, chemistry and microscopy.

Outdoor:

Walking, hiking, camping, fishing, hunting, boating, exploring, sports, mineralogy and nature study.

Group:

Dramatics, hobby clubs, study groups, and actual work in organized charities.

Group activities should occupy a large part of the adolescent's time, since it is vital for him to learn how to get along with others. Although a continual round of group activities may keep him from learning the value of quiet concentration and serious thinking, in the absence of many group contacts there is the very serious danger that the patient may develop a shy, withdrawn, introverted personality that is conducive toward dementia praecox (schizophrenia). Extracurricular activities at school, — clubs, orchestra and debating and dramatic societies, — church social groups, special organizations such as the Y. M. C. A., Y. W. C. A., Boy and Girl Scouts and their junior divisions, and the National Guard or similar military organizations all utilize the physical and mental energy of the adolescent, besides socializing and maturing him.

Sports are almost a fetish in this country, at least from the competitive standpoint. The tendency is for the quickest and strongest, because they make up the "school team," to have all the advantages of organized sports. Recently, the insistence on intramural sports in which all the students get a chance to play the commoner sports with those of their own general skill has done much to democratize sports. As much accent should be placed on "durable" sports, such as tennis, golf and hiking, which the player can continue when he gets older, as on intensely group-competitive sports, such as football, baseball and basketball. Also, the competition should not outweigh the sheer fun and relaxation inherent in sports.

Keeping a *diary* is useful in selected cases to get a better understanding of the adolescent, who can often write about his troubles better than he can talk of them. One should rarely use this method in the very introspective adolescent, since it will make him more so and such patients are difficult in the first place. A compromise method is note-

taking, in which the adolescent jots down at odd moments the things that he considers most difficult for him to understand or seem to produce unusual emotional reactions.

*Modifying the family situation*⁶ is necessary in practically every case, this procedure being omitted when the adolescent comes spontaneously and sometimes secretly so far as the family are concerned. Since the parents are usually the source of financial support, one must postpone fee expectation until the adolescent permits his parents to know that he is seeing a physician, or let the bill go indefinitely until he himself can pay. If the adolescent allows his parents to know, and in serious cases one may occasionally seek a secret conference with a parent, it is usually necessary to advise a modification of the parents' attitude toward the child. The parental attitude may have been condemnatory, prying, sarcastic, nagging or cold. The fault is seldom all on the adolescent's side, often, all he needs is a little wise neglect and absence of parental overattention.

A disconcerting fact, but one that does not negate the recommendations given above, is the observation that the parents are essential in preventing the development of criminally delinquent adolescents. The Gluecks⁷⁻⁹ found that in 60 per cent of 500 young criminals and in 58 per cent of 500 delinquent women there was a background of broken homes. If a parent is abusive or domineering or alcoholic, the adolescent will have trouble adjusting himself, both because he is antagonistic to the immediate situation and because his personality has been scarred through childhood by the baneful influence of such a parent. If the family situation is unusually bad, it may be advisable to recommend a foster home or care by congenial relatives.¹⁰ In planning the removal of the adolescent from the home, Rogers¹¹ points out that success will occur if the patient finds emotional security, a sense of acceptance and a relief from fierce sibling rivalry, and if his emotional ties to the parents are not strong. Rogers concisely charts the criteria for consideration in foster placement, although chiefly used in children, they are in a large measure applicable to adolescents.

The classic adolescent behavior of horseplay, loudness of speech, atrocious manners, airs of superiority and righteousness and constant criticism of everyone else is a trial to those about him but also an indication that he is a trial to himself. Much of this behavior is overcompensation and excessive assertiveness to bolster his feelings of uncertainty and inadequacy as rapid physical and emotional changes are occurring within him. Parents need reminding they were once quite as difficult, and that they should extend to the adolescent tolerance,

not ridicule, patience, not instability, and leniency, not annoyed discipline. By their wise handling of the adolescent, they can minimize the resentment and rebellion too commonly found in this period of life. They can foster his social adjustment by acting as sympathetic counselors, not as meddlers or dictators.¹²

Garland¹³ makes the following comments:

Restrained and inarticulate, the adolescent no longer reveals his innermost thoughts at home and thus fails to benefit from the safety valve of a confidential relationship with the parent. The parents have also their reticences. The father, even if he recognizes the desirability of it, cannot talk to this strapping and somewhat arrogant youth as that individual needs to be talked to, nor can the mother approach the daughter according to her needs.

The adolescent needs some kind of adult companionship that is free from family inhibitions. "It may frequently be the physician who can best serve as parent substitute, and particularly the pediatrician, if he has dealt wisely with his patients during their childhood. In this terra nova of medical interest he has early staked his claim."¹⁴ Parents may make the adolescent worse by dominating and overprotecting him; regardless of whether their children find them interesting or boring, companionable or indifferent, just or unjust, sooner or later the children will and should leave home.

Sex education should have been taken care of by the parents during the childhood years, but it is a wise rule to get from the adolescent his ideas on anatomy, physiology, coitus, pregnancy, childbirth and venereal disease. One should question closely but gently and should not be fooled by what is usually a superficial knowledge given in glib answers, for the investigator is frequently amazed at the half truths and gross ignorance of the adolescent, who depends on street talk for his sex education. A frank discussion of sex opens the way to a calm introduction of the often highly emotionally charged topic of masturbation, and provides an excellent opportunity to desensitize the adolescent on this matter. If the parents bring to the office an adolescent with a history of troubles about masturbation or what seems to be a homosexual situation, a safe and effective way to introduce the material is to tell the patient that when his parents were young anything about sex was considered scandalous, and that many parents get upset about such things and exaggerate them. As a rule, this approach makes the adolescent realize immediately that the physician is not the usual critical adult but an understanding person who does not automatically condemn him as an outcast or abnormal. The homosexual situation is usually found to be a harmless crush on an older person of the same sex, although the relation may

have been prolonged unwisely. If the adolescent has been caught in a homosexual act, he and the parents should be told that it is only a carry-over of sex curiosity and experimentation from childhood or a substitute expression of sex drive in a person whose sexual maturity has not yet reached an adult heterosexual stage. If the homosexual behavior persists or the adolescent is definitely effeminate—or masculine if the patient is a girl—in appearance and manner, he should be referred to a psychiatrist.

The most obvious obstacle during adolescence is the acquisition of heterosexual stability. It is in sexual matters that one has the most difficulty in getting an adequate history from the patient; it is a subject requiring great tact and patience, particularly with girls, and the information is often unobtainable until the emotional retention results in an explosion in a panic reaction or in a hysterical episode. Despite the so-called "frankness" of modern youth, the adolescent is often reluctant to admit that he is troubled about sexual matters. Thom¹² states, "By the time the psychiatrist sees the adolescent who is having conflicts over sex, the situation has usually become involved and invariably there has been considerable elaboration of incidents which in themselves were not particularly important." The family physician can head off the development of such conflicts if he is alert and able to devise means to have the adolescent come to him spontaneously and early in the trouble.

The stages that a person passes through before reaching healthy adult heterosexual development are as follows: an interest primarily in himself, accompanied by self-exploration and resulting in autoerotic practices common to all infants and young children; an interest in the differences between sexes, with some indiscriminate sex play and no preference for a particular sex, characteristic of childhood; an interest primarily in those of the same sex, characterized by "crushes" and hero worship, together with antagonism toward the opposite sex—these attitudes are found in early adolescence; and finally, in mid-adolescence, an interest in the opposite sex begins as "puppy love" and proceeds through late adolescence to adult heterosexual maturity.

The crushes and hero worship of early adolescence are evidences of transient homosexuality, which is unconscious and normal and seldom reaches overt expression, or of experimentation, if such activity occurs. When "puppy love" appears, the adolescent is usually well on his way to successful heterosexual adjustment. Should the unconscious homosexual stage be prolonged beyond the age of eighteen, some investigation is indicated, since superficial causes, such as inability to dance,

fancied or actual ugliness of face or body and lack of suitable clothes, may be keeping the heterosexually inclined adolescent from taking the plunge into the social affairs necessary for contacts with the opposite sex. Aldrich and Aldrich¹⁵ write as follows:

If it were possible to keep to the perfect letter of our social regulations, youth would grow up without experiencing any sexual feeling at all until marriage, at which time they would be expected to adjust successfully to this complicated growth process . . . when the maturing child feels the normal quickening of his sexual life, memories of those early punishments (shamings and spankings for childhood sex play) come up to make him feel ashamed and guilty instead of giving him a basis for security and satisfaction in the growth of his ripening powers. An appreciation of sexual competency as a constructive asset is a high and difficult standard for children to attain in our inconsistent world.

Career ambition needs attention, not just actually to pick out the best suited for the particular adolescent but also to keep him interested in the future along with a reasonable amount of self-evaluation (physique, intelligence, any unusual ability, education, maturity and so forth) to keep at a minimum the wild selection of impractical careers so common in early adolescence. It is useless directly to dissuade the adolescent from a certain career goal, no matter how absurd or impossible it may be; however, by reviewing with him his assets and liabilities in reference to the desired goal and encouraging him to investigate the years of training needed, one can often get him to abandon or modify his immature ambition. Equally important is the procedure of leading him into serious and mature planning for his career selection when such a selection is in keeping with his abilities. The adolescent with average intelligence should take a high-school course that will be useful in office work and the trades, and should not spend his time on the classics of a college preparatory course and be left on graduation day with much impractical knowledge so far as getting a job in everyday life is concerned. One should impress on him the value of night school to further his education while he is supporting himself. Jobless youths are serious problems, and it requires real ingenuity to devise and find ways to keep these young folks occupied, to prevent delinquency and loss of self-respect. They should be urged to do charity work, attend almost any of the free courses that most cities offer, or investigate the NYA and CCC projects, as well as military service—anything to keep them busy. Many parents, and consequently their children, still have caste ideas concerning the "trades" in contrast to white-collar jobs, and may ignore valuable advice about the study of a trade.

Delinquency refers to antisocial behavior that is considered criminal, such as habitual stealing, destruction of property, vagabondage and running away, occurring in children under the age of sixteen in most states. As mentioned above, genuine psychopaths, of which true juvenile delinquents are but smaller editions, are very serious problems and should be referred to the psychiatrist.¹⁶ Meanwhile, there is too great a tendency to label as a juvenile delinquent any youngster picked up by the police more than once. Too often, the child or adolescent has against him several minor charges that are reflections of obviously unhealthy environment—slum sections, broken homes, idleness, poverty—rather than vicious antisocial behavior from character defects. Thom¹⁷ concisely outlines modern thought and trends concerning delinquency, and indicates the value of mental hygiene. "I believe that until mental hygiene can be reduced to such terms that it can be utilized in the everyday practice of parent, teacher, nurse, physician, probation officer and others concerned with the training and education of children, it will not serve a useful purpose." Much so-called "delinquency" needs only careful analysis of motives, the offsetting of such etiologic factors as poverty, disease and idleness, and the redirection of the adolescent into healthy activities (clubs, camps, sports, hobbies and recreation) under mature guidance of counselors, playground directors, Big Brothers' and "Big Sisters," or similar mentors. Healy and Bronner¹⁸ have reported most encouraging results in a series of 400 cases treated at the Judge Baker Guidance Clinic five to eight years before the follow up survey. They record 81 per cent favorable results in nondelinquents,—that is, children with the less severe personality and behavior problems,—and 70 per cent favorable results in delinquents.

Feelings of inferiority may be inferred from the adolescent's behavior (aggressiveness, noisy conduct, shyness and aloofness), or the cause may be described by him as frail body, clumsiness, stupidity, inability to dance, acne, inadequate clothes and so forth. Each point can be handled by explanation, by reassurance and, particularly, by a reference to similar difficulties endured by other adolescents. Adolescents are often sensitive to wearing secondhand clothes, and should be allowed some new ones occasionally, at least the 'Sunday best' outfit should not be a castoff. Often, the social and economic levels of the family may be sensitive points as the adolescent compares them with those of his friends and acquaintances. He may resent or feel ashamed of what he considers a class inferiority because of such factors as car, clothes, church affiliations, portion of town in which he lives, size of house and whether rented or owned, size of

allowance, and social status as shown by clubs and societies in which his parents may or may not hold memberships. He should be desensitized to avoid snobbery, and the reading of appropriate biographies will promote a realistic sense of values.

Chronic invalidism or prolonged convalescence, as in acute or severe chronic rheumatic fever, pulmonary or bone tuberculosis, anterior poliomyelitis, chronic pyogenic osteomyelitis and amputations, presents a crying need for mental hygiene precepts and psychotherapy. The ingenuity and patience of the physician are often taxed to keep these adolescents occupied, interested in daily life, cheerful, unselfish and free from self pity. An attitude of gently humorous interest in their case and encouragement to follow several practical activities or hobbies will sustain these young folks for months. In the community, facilities may be available for interesting and instructive 'visiting services,' such as social work, teaching, occupational therapy and voluntary reading and games with invalids. At times, it may be necessary to advise care in a foster home¹⁹ because of crowding or a severe personality clash between the invalid adolescent and some member of the household.

Consultation with the school authorities may be advisable when behavior or scholastic difficulties beset the patient. Again, one must use tact and often secrecy in such contacts, otherwise, the adolescent may believe that the physician is violating his confidence or is siding with the school. When the necessary history has been obtained from the school officials and the problems outlined, the physician should recommend indicated changes in school curriculum, suitable disciplinary methods and his own general plan for handling the situation directly with the patient.

In conference with the school authorities, one can often profitably suggest inclusion of sex education material²⁰ in courses, such as biology, physiology, hygiene, physical education, sports and sociology. Personality clashes between teacher and adolescent should not be taken seriously provided investigation does not show the teacher to be a misfit. The adolescent must be quietly impressed with the reality that all through his life he will be under the authority of apparently disagreeable persons and must learn to "take it", in addition, he should realize that the personal problems of the teacher, such as financial worries, emotional disturbances, family stresses, and physical and nervous fatigue, may be solely responsible for the irritability and antagonism he shows the adolescent. Teachers²¹⁻²³ notoriously consider the relatively aggressive child a behavior problem because of his nuisance value, whereas the shy, withdrawn child is praised. Unfortunately the former is by far the healthier personality. As pointed out above,

regarding the parents, it is often not the adolescent who needs all the guidance and correction: those in contact with him need considerable education in mental hygiene.

Marriage of an adolescent does not automatically make him an adult, no matter what the legal attitude may be. If the marriage is permitted to continue, both the adolescent or adolescents and the parents need help to smooth the personality adjustments necessary, particularly when there has been an elopement. The adolescents are grateful for advice concerning special adjustment and the question of pregnancy, and many nonmedical problems, such as living with parents, whether both adolescents should work, life insurance, and even budgeting and homemaking. In turn, the parents need desensitization to their "in-laws," and often must be restrained from seeking legal redress or disowning the adolescent when such actions solve nothing and only make the situation worse. Unfortunately, the physician's influence is seldom sought in such matters.

Contact with pornographic literature, a common experience in adolescence, varies from crude sketches and verses on sidewalks and toilet walls to "French postcards" and lewd cartoon books. That this is not a more serious problem is a compliment to the adolescent, or perhaps it is because he is desensitized by the prevalence of sex appeal in modern motion pictures, magazines and advertisements. The more overt occurrences respond to matter-of-fact discussion with those involved; one appeals frankly to reasonable standards of personal ethics and good taste, and makes specific efforts to locate and deal adequately with the adults who are supplying such material to the adolescents. Making a humiliating example of such youthful offenders or preaching with righteous indignation does little good.²⁴

Dishonesty, including lying, cheating in examinations and stealing, should be handled in a similar manner. The motives for such conduct, of course, are important, since etiologic treatment is always best. Cheating may be based on attempts to maintain high grades or pass in school subjects demanded by parental ambition, or may be prompted by laziness or boredom. Stealing may be a means to obtain desired luxuries or money to buy favors and win attention from associates when inferiority or handicaps prevent satisfactory competition otherwise.

Since the adolescent must learn to adjust himself in community life, every possible community faculty should be employed to interest him and occupy his energies. Thus, the physician should keep in mind the availability of clubs, training projects, hobby groups and so forth.

Concerning psychotherapy in general, the following realistic evaluation of Kanner²⁵ is pertinent:

For psychotherapy, regardless of dictionary definitions, is not a sectional procedure, a trick, a technique, or circumscribed method, a selected emphasis addressed to an unconscious, a complex or any other personified abstraction. Practical psychotherapy is the organized treatment of a person in trouble, uniquely adapted and readapted to a unique person and a unique situation. . . . Its ideal goal is the adjustment of all that is maladjusted in an individual child and his specific environment; its working endeavor is the adjustment of all that can be adjusted at a given moment. It steers clear both of Pollyanna sweetness and nihilistic bitterness. . . .

CASE HISTORIES

CASE 1. C. D. F., a 19-year-old boy, reluctantly went to a psychiatrist with a complaint of constant fatigue and lack of energy. He was well developed and nourished, and had the physique of a football player. He left college in the second year to go to work, and had his own used-car business on a small scale but made a fair living. His complaints of fatigue, lack of energy and aching all over had been in evidence for years, and he did not recall ever feeling "pepped up." There were no hypochondriacal complaints, and he was humorously aware of the discrepancy between the complaint of fatigue and his strong physique. The history showed an extremely dominating, querulous, attention-craving father who was very successful in business, but who was a mass of hypochondriacal complaints and spent two or three months each year going from one health resort to another. The mother, an unusually pleasant person, understood the father and tried to offset the terrific tension that his presence constantly maintained in the household. This tension was so severe that the patient's younger brother (Case 2) also required psychiatric help. An older brother, after years of clashing with the father, had left home, and during 3 rather stormy years of trying to get settled with a job and a wife, had also needed psychiatric help. The patient had never taken an active interest in sports and never did much physical work. The social adjustment was good with adults but only fair with his colleagues, since his constant feeling of fatigue made it an effort to take part in dancing parties, swimming parties, picnics and so forth.

Treatment consisted in an insistence on a gradually increasing program of physical activity, including a Y. M. C. A. membership and joining a hiking club, which took the patient on cross-country hikes and amateur mountain climbing at least twice a month. The effect of his father's personality was explained, and the patient saw for the first time the whole situation so far as intra-family attitudes were concerned. With this insight, he said: "I think we are all fighting against the old man. He never went to college but has always said that he would give his boys a college education. As a matter of fact every darned one of us [3 boys, aged 24, 19 and 18] have quit college despite the old man's objections." This was exactly what had happened; the only son who had completely rebelled was the oldest, who had left home.

CASE 2. D. R. F., an 18-year-old boy who was referred to the psychiatrist by his brother, C. D. F. (Case 1), was a slender, restless, obviously tense boy who talked rapidly. His story concerning the father's influence on the children

was essentially the same as that given by his brother, but he added: "The old man gets me down more than the others now, probably because I am the youngest. I am high strung like he is anyway, and he nags and criticizes me so much that I feel just no good."

The patient worked during the summer in a small store owned by the father, and enjoyed meeting people and serving them. Such work had given him a sense of self confidence and made him feel useful. The father in the meantime, regarded keeping the boy a clerk in the store as excellent discipline. The patient recognized this motive and was somewhat amused by the fact that instead of being disciplined and under the control of the father he was actually in the best environment to get away from the constant feeling of insecurity that his father's influence thrust on him. The patient said that he was entering the second year of college but really wanted to go to work in some business in which he would have contact with people and give service. He stated that he was going to leave college about Christmas time, although he dreaded the scenes his father would put on when he heard the news. His next words were practically an exact quotation of what his brother had said during an interview: that the father felt inferior at not having gone to college and was obsessed with the idea of giving his children college educations.

From what his brother had been told the patient had developed insight into his own nervousness and treatment consisted chiefly in more explanation and a great deal of reassurance.

CASE 3 H L A 16-year-old girl was referred by a dermatologist after he had been told by the parents that the girl seemed very depressed. He was treating her for marked acne vulgaris of the face, neck and shoulders and she had been referred to him by the family physician whose efforts for several months had not helped the skin condition. The patient was very well developed and nourished with good facial features, except that her nose was somewhat flattened. Posture was good and her carriage in walking was unusually good. There was marked acne over the face with many areas of folliculitis and a moderate degree of scarring. She was in the junior year of high school and had active interests in basketball, dramatics and church activities. She did not care for dancing and had not yet had any special love interests.

The patient admitted that her feelings of depression were due to sensitivity concerning her complexion. She frequently noticed people looking at her because of her skin condition and the boys and girls at school sometimes teased her. She often cried to herself particularly at night and although she did not avoid group social contacts she did not seek any more than went along with her school and church activities. She definitely avoided dates with boys.

Treatment consisted of reassurance and explanations for the acne. The patient was informed that glandular overactivity, which is so common during the adolescent period, was responsible and that the lesions would eventually regress. She was desensitized against awareness of people looking at her by the statement that her excellence of figure, carriage and poise were probably as much responsible for people noticing her as her poor complexion. It was suggested that her disinterest in dancing was based as much on her awareness of being a poor dancer as it was on her sensitivity about her face. She was advised to use every opportunity to dance and the parents made arrangements for her to take lessons in ballroom dancing. Her life situation was formulated as follows. Since she

was interested in business and secretarial work, and for the next 3 years her main job would be to finish high school and get a year of business college, she should point her main efforts in this direction. In the meantime she was to improve her dancing and constantly keep in mind that despite her temporarily poor complexion, her assets of physical attractiveness were unusually good and that a year or so later, when her skin condition had subsided, she would be a very pretty if not beautiful girl. Incidentally, she was reassured by the psychiatrist and the dermatologist that whatever scarring remained could be removed by plastic surgery.

This particular case was properly handled all along the line although the family physician was somewhat slow in referring the case to the dermatologist. The most important points in the psychotherapy were that the skin condition was an annoying human experience and that the patient's physical attractiveness and personality were definitely superior and would not be particularly impaired by the facial blemish.

CASE 4 N C An 18-year-old girl, had had practically constant nausea and frequent bouts of vomiting for 3 years beginning shortly before an uncomplicated appendectomy. She had a brother 2 years her junior who was in the same class in school and there was a good deal of rivalry between them. The patient's symptoms of nausea and vomiting were always aggravated by any change, such as that caused by visitors and trips. Once or twice she had fainting episodes in school. For the previous 2 years, she had done practically nothing except go to school; she was waited on by her parents and was not even required to pick up her own clothes. Examination showed a very well developed and well nourished girl who was emotionally quite immature and talked and acted like a high school freshman.

After the nervous origin of the nausea and vomiting had been explained, a program was outlined with the parents in which the girl was to assume an increasing number of duties and responsibilities about the home. She was made to care for her own room, do ordinary sewing, get breakfast and plan the other meals, and do all the marketing. There was no open rebellion at these tasks, probably because it was explained that she would not be permitted to enter college—where she had already been accepted—if she did not follow directions in detail. Within a month on such a program there was a marked change in her general poise, the chatter and juvenile restlessness of the usual 14-year-old which had been her general behavior faded into the appearance of a fairly quiet and more or less serious girl of 18. She was beginning to take pride in the household responsibilities, experimented with new menus and had done some original and inexpensive interior decorating in her own room. The symptoms of almost daily nausea and vomiting were quite stubborn and it was another month before any particular change was noted. These symptoms slowly subsided within the next 6 months and now occur only once in 2 or 3 weeks.

CASE 5 G J A 19-year-old boy, was oversensitive and oversolicitous concerning his health. Limited exercise to avoid fatigue went to bed early each night to get at least 10 hours of sleep, was fussy about his diet and ate various types of popular health foods. Throughout high school he had frequent bouts of vomiting for which an organic basis was never found despite repeated examinations. The history of the vomiting spells showed definite association with nervous tension and a feeling of inferiority to his fellow students both scholastically and so-

cially. He did well in his studies in his freshman year at college, and during the first half of the year there were no spells of vomiting. As the year progressed, however, the vomiting returned, and during the summer vacation, the family physician, concluding that the vomiting was functionally related to the school situation, recommended that the patient travel or work for a year and then return to school. The diagnosis was only partially right, since after the first few weeks of an office job, the vomiting returned, and the family physician referred the patient to a psychiatrist. Another symptom, insomnia, had developed, and in addition to his overconcern with his physical health, the patient felt he would lose his mind because he was not obtaining adequate sleep.

He had been reared on a farm, the youngest of four boys; the oldest brother had taken charge of the farm at the father's death. The other brothers imposed on the patient by giving him much more work and responsibility than his years warranted because he was very faithful, being the first one up in the morning and the last one to retire at night. He had therefore practically no normal late childhood and early adolescence from the standpoint of carefree play. The case was thoroughly reviewed with the family physician, and a program of psychotherapy and occupational therapy outlined. The chief points in psychotherapy consisted in reassurance about his health and particularly about the problem of sleep, and in the development of an insight regarding his excess of seriousness, conscientiousness, health consciousness, reserved attitude and self-criticism. Occupational therapy was directed toward hobbies of the group type, to foster social ease. After several months of membership in a hiking club and a photography club, the patient made several valuable friendships and acquired self-confidence in social situations. In the 2nd month of treatment (an hour interview once a week), the vomiting ceased and sleep improved; at the same time, he found his office job much less irksome. He returned to college and has made a very satisfactory adjustment; he is still inclined to be rather shy and a bit overcareful concerning his physical welfare, but his original condition is much improved.

CASE 6. R. S., a 20-year-old high-school graduate, had been married for 2 years and had 1 child (aged 18 months). At the age of 14, this boy lost his left arm at the shoulder from an automobile accident. He was the older of 2 children and was always the mother's favorite; his disability increased the amount of attention from her, so that he became spoiled, sulky, demanding and self-pitying. He took no part in sports or hobbies; his parents gave him a car and plenty of money, and most of his time was spent on parties, drinking and racing around the countryside. His girl friends were of an inferior type socially and intellectually, obviously because he felt more comfortable in their presence and because his money and his car made a great impression. He eventually had to marry a girl because of pregnancy; she had only a sixth-grade education and worked as a waitress at a very inferior type of tavern. The boy's parents, after this episode, were amenable to reason, and realized that their oversolicitude had been to a great extent responsible for the boy's warped personality. He had never been taught to compensate for his physical handicap. The parents accepted the girl and at first had the couple live with them, but after the baby came they very wisely set them up in a home of their own.

The boy is still far from well adjusted but is trying to accept advice and responsibilities. Treatment consisted of explanation, reassurance, praise and criticism carefully

blended, and a definite program of work, social contacts, hobbies and a continuation of his and his wife's education through planned reading and night school.

CASE 7. H. C., an 18-year-old college freshman, had been getting drunk about once a month since the age of 15 and had been dismissed from two preparatory schools because of his drinking. He was very reserved and found that alcohol made him able to mix socially with comfort. He was the youngest of 4 children, all boys, and there was 8 years between him and the next older brother. The father was a West Point graduate, domineering, aggressive and a very successful businessman. There was considerable army tradition in the family; several ancestors and a brother were West Point graduates. The boy qualified for West Point and passed the entrance examinations, but was turned down because of defective vision. This was a great disappointment to him and also to his parents. The mother was a vivacious, attractive woman, of Spanish ancestry, and temperamentally the opposite of her husband; she had spoiled the boy in her efforts to soften the father's treatment of him. The college authorities had noted a gradual decrease in efficiency, withdrawal from social contacts and a facial expression of depression. The college physician found nothing organically wrong and entirely missed the psychiatric implications, so that the boy was sent home with a medical opinion suggesting that he was lazy and needed disciplining. This, of course, only made the father's attitude severer, and for a while he kept the boy home studying; as a result, the patient became more and more withdrawn and depressed. On two occasions, there was suggestive evidence that he had made suicidal attempts—the first by an overdose of codeine, and the second by illuminating gas. The boy would not admit these, but the mother was sufficiently alarmed to refer him to a psychiatrist.

The history given to the psychiatrist was almost classically that of a slowly developing schizophrenia, and the prognosis appeared poor. On examination, however, the psychiatrist noted that the boy, although appearing disinterested and apathetic, within a relatively short time made a very active transference to the physician and soon poured out his story. Another factor that made the prognosis much more hopeful and entirely changed the diagnosis was the significant observation by an attendant caring for the boy at home that when the parents were out of the house for several hours the patient turned on the radio, at times hummed or whistled in an alert, buoyant manner, and occasionally laughed quite cheerfully. At no time was there any evidence that this boy was malingering; it seemed that the father's presence was a dark cloud, which immediately overshadowed the boy's usual state of average adolescent spirits.

The boy gave the following story to the psychiatrist: "For a year and a half, I have lost all interest in things [the West Point disappointment occurred at about the time of the onset]. I had no more emotional reactions to anything. In college, I studied hard but gradually my concentration got worse. One night I spent from 8 p.m. to 4 a.m. going over one or two paragraphs without being able to understand or remember the contents [his marks in preparatory school had always been high and he had a superior intelligence]; this scared me. I quit school and went home by hitch hiking, but got drunk on the way [in a little town near his home, as though he sought alcoholic courage before facing his parents] and spent a night in jail. My father raised hell; he made me stay in all the time and study. He wouldn't let me see my girl

[the patient was in the middle of an intense love affair, of the usual idealistic, adolescent 'puppy love' variety], and I worried about another fellow taking her out. All I do is hang around the house, usually in my room. I don't care to see anyone, and I don't want to do any thing but read or sleep." There were no hallucinations or delusions, ideas of reference or feelings of being controlled.

Therapy in this case was difficult and not very successful at first because he was kept at home. The parents tried to be co-operative, but the father considered the boy's symptoms "all a bunch of damned foolishness—all that boy needs is a few good beatings." The boy was given a great deal of freedom, the relaxation of restrictions at first seemed to help him, but he soon became quite reckless in behavior, winding up in jail for drunken driving. It was apparent that a return to personal freedom should be made more slowly and in a neutral environment, and he was therefore sent to a private sanatorium. It was subsequently learned that although the father gave the boy the freedom recommended by the psychiatrist he stood in the background and constantly glared his disapproval of the boy's actions and often muttered threats and curses under his breath. This attitude, of course, only made the patient more and more panicky, increasing his recklessness as he tried to get in as much fun as possible before the father clamped down on him again. The boy's adjustment in the sanatorium was excellent, and he rapidly developed insight into the emotional turmoil in which he had lived for about 2 years. After 6 months he returned home to approximately the same parental situation, but he was able to withstand the father without an open clash and also without building up a store of resentment. He re-entered college and is successfully completing his freshman year. It is quite possible that the 6 months of hospital care would have been unnecessary if the college physician had been able to get the boy's confidence and learn the whole story or had recognized that the boy was in an emotional turmoil and referred him to a psychiatrist.

CONCLUSIONS

An analysis of the problems of adolescence is presented, methods of psychotherapy are outlined, and appropriate case histories are discussed.

The adolescent must gain independence and freedom from parents; he must learn to take re-

sponsibility for himself and to some extent for others; he must learn the value of money; he must learn to live with others, to make a comfortable social adjustment and to respect the rights of others; and he must have a reasonable goal of successful adulthood regarding education, economic stability and psychosexual maturity.

Adolescents with chronic illnesses or crippling physical defects are especially in need of psychotherapeutic attention.

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Erratum. In the paper "Deterioration of Milk by Bacterial Growth Under Refrigeration at 40°F," by Frank E Mott and Henry Mazer, in the July 30 issue of the *Journal*, three errors appear on page 174: the abbreviation "C" in line 21, column 2, and in the two subheadings in Table 2, should be changed to "F."

MEDICAL PROGRESS

KIDNEY DISEASE

REGINALD FITZ, M.D.*

BOSTON

TWO excellent reports on recent medical progress as it concerns renal disease have already been published in this year's series; both are by Dr. John H. Talbott,^{1,2} of the Massachusetts General Hospital. In one, he discusses modern tests for renal function and describes methods now being employed to investigate glomerular filtration and effective renal blood flow. To read of Diodrast and inulin clearance tests as they are now employed makes older clinicians like myself a trifle nostalgic. Thirty years ago, I spent the summer in Tübingen, working with Carl Schlayer. His researches were pointed in the direction of studying tubular and glomerular function, as a test for the one potassium iodide clearance, and for the other, lactose clearance being used. Smith³ has now gone ahead much farther along this line, adopting for the same purpose a different iodine compound and a different sugar. His methods are being tried in different clinics and appear to offer interesting results. As an example of the kind of work going on with these methods, Dill, Isenhour, Cadden and Schaffer⁴ have studied renal blood flow in the toxemias of pregnancy, concluding that the same fundamental vascular abnormality is responsible for hypertensive disease as for toxemia.

There is still debate regarding how much the rate of blood flow through the kidney is impaired by hypertension per se. Dock⁵ has attempted to explore this angle of the renal problem by perfusion experiments. He believes that kidneys from patients with hypertension have vascular beds that are within the range of normal and that therefore renal arteriosclerosis is rarely a cause of hypertension, although he admits that this may be a secondary complication.

Talbott's second paper discusses what he terms "heterogeneous renal disorders." He describes a variety of unusual renal disorders that are of considerable interest to the man who may be more concerned with the clinical side of nephritis than with renal physiology.

The war has already brought to light two forms of kidney disease that have hitherto received no great attention. Gilligan and Blumgart⁶ have dis-

cussed what is termed "march hemoglobinuria." This medical curiosity, no doubt, occurs much more frequently than is generally believed.

Nine years ago a patient of mine, hitherto always able to exert himself without trouble, suddenly developed what appeared to be bloody urine after playing a game of squash. A few days later, the hematuria recurred under the same circumstances, and the patient consequently gave up such a violent form of exercise. Some time later, however, after a gentle outdoor run, he developed a third attack of what seemed to be painless hematuria. Complete urologic studies, including cystoscopy and retrograde pyelography, were made, with completely negative results. Since then, the patient has played golf and mixed double as he chose, with complete impunity. Many specimens of urine have been examined, and they always have been entirely normal. I suspect that the patient had an attack of so-called "march hemoglobinuria."

Gilligan and Blumgart have made an excellent clinical study of 3 such cases. Their article is worth reading not only for its informative value but also for the delightful manner in which it is presented. Briefly, the 3 cases were studied most meticulously in a variety of ways. The authors conclude that march hemoglobinuria is a form of paroxysmal hemoglobinuria already well described. It occurs in attacks in otherwise healthy persons following walking or running, and may have something to do with the mechanics of body posture. There are usually no symptoms or very slight symptoms with attacks. The paroxysms appear to be due to intravascular blood destruction rather than to any extrinsic cause, and no great amount of blood is destroyed at any one time. Spontaneous recovery is the rule.

This study has been presented at a very opportune time. Gilligan and Blumgart predict that this type of paroxysmal hemoglobinuria will soon attract much more attention than ever before because of the large number of young men who are engaged in the strenuous exertion of military training. During the next few months, therefore, other cases will doubtless be presented. The value of having the condition in mind and of differentiating it from more serious conditions leading to the passage of blood-colored urine is obvious.

In the *British Medical Journal*, two interesting papers^{7,8} described the peculiar renal changes that complicate severe crushing injuries. People so injured are likely to develop, in the course of a few days, a very striking renal lesion characterized

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual*, Vol. III, 1942 (Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

*Lecturer on the history of medicine, Harvard Medical School.

clinically by generalized edema, oliguria, acidosis, a rise in the blood urea nitrogen, a retention of blood phosphorus and potassium and a fall in blood sodium and calcium. The prognosis is always uncertain. The fatal cases that have been examined have shown a degenerative lesion localized chiefly to the collecting tubules and not unlike the type of acute nephritis that may develop after improperly matched blood transfusions.

Knowledge concerning this disorder has developed very quickly. In the first place, as so often is true when something new in medicine appears to be uncovered, the condition has already been fairly well studied. It seems ironical that Minami,⁹ in 1923, who seemingly was then a Japanese student working in Pick's laboratory in Berlin, should have been the first to publish a comprehensive review of the subject. It is clear, however, from this paper that during World War I the Germans were thoroughly familiar with the peculiar syndrome that may follow crushing injuries, although why no attention was paid to the matter by American and British officers is less certain.

During the present war, the British have again been impressed with the crush syndrome, and, through the use of methods that were not available to previous workers, have added much to knowledge concerning it. Several hypotheses regarding its cause have been presented. Robertson and Mathews¹⁰ have given an explanation that now is generally accepted: a crushing accident interferes with the circulation in the affected parts, and there is considerable muscle damage. A substance called 'myohemoglobin' is set free, is absorbed in to the general circulation, and passes to the kidney. Glomerular activity is reduced by this foreign substance, and tubular flow is diminished. As a result, myohemoglobin is concentrated in the tubules, with the formation of casts. Thus, it seems probable that acute nephritis from crushing is due to mechanical obstruction by myohemoglobin and also, probably, to some other unidentified toxic substances that are formed.

Several forms of treatment have been developed. On the theory that the syndrome is due not only to the liberation of toxins from the crushed tissues but also, in part, to loss of blood constituents into the injured limbs, treatment with intermittent positive pressure has been attempted. The treatment of the infection or the gangrene that so often accompanies the crush has also been attempted by the use of various more or less radical surgical procedures on the theory that pressure in deep and badly injured muscle compartments may add to the damage to tissues. Alkalization and the intravenous injection of fluids in various forms—including, most recently, glucose in isotonic sodium sulfate solution—have been advocated.

Adrenocortical hormone has been administered because of the high blood potassium levels frequently encountered. Of course, transfusion with whole blood, serum or plasma has often been used. The crush syndrome is so serious and its mortality is so high that careful clinical or experimental studies dealing with it may prove to be extremely valuable.

I can recall once having seen a patient in the Peter Bent Brigham Hospital whose legs were badly crushed in an automobile accident. I suspect that he developed the form of renal lesion that now so much interests the British medical officers for within 48 hours after the accident and for no apparent cause, the blood urea nitrogen was 61 mg per 100 cc.

The patient developed a gas-bacillus infection lost both legs and later acquired an indolent intractable anemia, which lasted for several weeks, a finding said to be characteristic of the crush syndrome. He is now alive and well.

Detailed reports of similar cases more carefully studied in civilian hospitals would be helpful in developing better methods for the treatment of this type of casualty. Unfortunately, so long as the war continues, the syndrome is likely to be encountered often, and certainly, as judged by the British experience up to date, it is serious. Husfeldt and Byering¹¹ have demonstrated that civilian hospitals afford a chance to study a problem of this nature. A few cases carefully observed in the tranquil atmosphere of civil life might prove enlightening, and surely the problem of injury from crushing can be investigated in the laboratory by direct experimentation.

So far as the peacetime aspects of renal disease are concerned, the literature of the past year, as usual, contains many interesting articles. If one wishes to get a bird's eye view of what surgeons are doing in the treatment of cardiorenal disease, a paper by deTakats et al.¹² is worth reading. Hypertension in certain cases can now be approached through surgery, provided that the correct diagnosis of the underlying cause is first established. Certain unilateral adrenal tumors, for example, may cause proximal hypertension, the removal of a unilateral atrophic kidney also affords a means of curing hypertension in a strikingly dramatic fashion, attempts to revascularize the kidney by tissue implants appear to offer some hope of success, and even the treatment of hypertension by splanchnic nerve resection is still under discussion.

Simeone¹³ has published a very interesting paper, which deals with the intelligent use of fluids in the care of men with impaired renal function due to prostatic obstruction. He points out clearly how essential the proper use of fluids is, and he comments on the various changes in the blood chemical findings that may occur. If these changes are interpreted correctly, they help to point out the type of fluid that should be administered and also

indicate the results of the therapy that is being pursued. This is a well-written, clear and comprehensive paper.

Endocrinologists have begun to study the kidney seriously. Selye¹⁴ has given an excellent review of the literature in this field and has added some experimental evidence of his own. He thinks it probable that the kidney is dependent for the maintenance of its normal structure on the balanced production of the growth and thyrotropic principles in addition to the effect of gonadotropic and adrenotropic hormones. Selye's paper is interesting to read, for if results obtained experimentally can be transferred to the clinic, it is easy to imagine many endocrinologic implications that might play a part in causing different forms of kidney disease.

To one who has heard the subject of nephrosis debated, a paper by Gilbert¹⁵ is refreshing. As is well known, there are two schools of thought: one is that nephrosis is a separate entity from which patients either recover or during which they die of intercurrent infection; and the other is that nephrosis represents simply a stage in development of the pathologic process that ends in clinical and anatomic chronic glomerulonephritis. Those who worked under Dr. Henry A. Christian have absorbed the latter belief. Gilbert reports a typical case of nephrosis, observed carefully during a four-year period, in which the pathologic findings characteristic of chronic glomerulonephritis were finally demonstrated.

It seems interesting, too, that the much debated topic of the effect on hypertension of a high-protein diet should still be worthy of investigation. Yet Philipsborn, Katz and Rodbard¹⁶ have once again demonstrated, this time on dogs, that these diets have no particular effect on the course of hypertension, although, of course, such diets may elevate the nonprotein elements of the blood nitrogen. At the moment, medical fashion appears to be in a phase of the cycle that is very far away from that of those days when the patient with hypertension was told, at all costs, to eat neither meat nor salt.

Anyone who has recognized hyperparathyroidism and has had the satisfaction of seeing a parathyroid adenoma removed will forever after maintain an interest in the intricacies of calcium metabolism. Andersen and Schlesinger¹⁷ have described 2 new cases of renal hyperparathyroidism and summarized current views on this subject. They make the point that there is a difference in secondary hyperparathyroidism from kidney disease as it is seen in children and adults. In young persons, the underlying renal lesion is likely to be congenital, whereas in the adult it may be acquired and the result of pyelonephritis, glomerulo-

nephritis or vascular disease. At all ages, the accompanying renal insufficiency is severe and chronic. At any age, in renal hyperparathyroidism, a moderate excess of vitamin D, at levels usually harmless, may produce hypercalcification of the bones and deposition of calcium in the tissues, including the media of the small arteries.

Besides its interest, another useful aspect of this paper is its bibliography. References are given to the first account of extirpation of a parathyroid adenoma as a means of treating osteitis fibrosa, to the literature dealing with hypertrophy of the parathyroid gland secondary to chronic renal insufficiency and, finally, to articles dealing with the close similarity between adult renal hyperparathyroidism and renal rickets.

* * *

As I have stated in previous years, I find it extremely difficult to write anything that approaches a complete report of current literature during a given interval on such an inclusive subject as renal disease. I have made no mention of the work going on with renin, on the effect of the sulfa drugs on the kidney or on many other aspects of kidney disease. Rather, I have tried to limit myself to comments on work, either old or new, that during the past twelve months has been of especial interest to my own tastes.

319 Longwood Avenue

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., Editor

CASE 28331

PRESENTATION OF CASE

A sixty-five-year-old man was admitted to the hospital because of jaundice.

The patient had been well until seven weeks before admission, when he had a so-called "streptococcal throat" for a week. During this episode, he received a twenty-four-hour course of sulfanilamide. He never fully recovered his strength and, three weeks prior to admission, noted for the first time the onset of painless jaundice accompanied by light stools and dark urine. The degree of jaundice did not seem to fluctuate, and during the two weeks prior to admission he complained of an "itchy skin."

Six years before admission, an appendectomy was performed because of pain in the right flank; the appendix was said to have been normal. The patient was told at this time that he suffered with kidney trouble. He had no further urinary symptoms until three years before admission, when, following an attack of left-flank pain, he noted dark-red urine that persisted for several days. After examination of the urine, a physician told the patient that it contained blood. The past history was otherwise irrelevant.

Physical examination revealed a well-developed, deeply jaundiced man, who complained often of itching of the skin. The abdomen was soft, and there was no tenderness. No masses were felt. The liver edge was not palpable. Examination of the heart and lungs was negative.

The blood pressure was 148 systolic, 92 diastolic. The temperature was 98.6°F., the pulse 100, and the respirations 21.

Examination of the blood revealed 70 per cent hemoglobin and a white-cell count of 11,600 with a normal differential count. A blood Hinton reaction was unsatisfactory. The serum bilirubin was 4.75 mg. per 100 cc. direct and 6.75 mg. indirect. The nonprotein nitrogen was 44 mg. per 100 cc. Examination of the urine was negative except for a +++ test for bile, a rare red cell and an occasional white cell. The stool was guaiac negative. The prothrombin was 33 seconds (normal, 18 seconds).

A gastrointestinal series revealed considerable spasm of the antrum of the stomach. The duo-

denum showed no evidence of ulceration or constant pressure defect. A barium enema was negative. A flat film of the gall-bladder area showed no definite evidence of stone.

Operation was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. F. DENNETTE ADAMS: This patient was doubtless operated on for biliary-tract obstruction. The history is somewhat meager, and before proceeding with a discussion of the case, I shall ask Dr. Mallory to inspect the hospital record and see if answers to any of the following questions are available: Was there anorexia, nausea or vomiting shortly after the acute upper respiratory infection subsided? Did the patient receive any form of medication other than the sulfanilamide? Was the spleen palpable? What was the differential count? Was there fever after the respiratory infection subsided? What was the color of the stools?

DR. TRACY B. MALLORY: There seems to have been a very slight degree of anorexia. The spleen was not felt. The polymorphonuclear count ranged from 70 to 90 per cent; there were no abnormal cells. Up to the time of operation, the temperature was normal, and the respirations were constant at 20. The single stool examined was reported to be dark brown.

DR. ADAMS: Would it be fair to ask the roentgenologist some questions before proceeding?

DR. MALLORY: Yes, at any time.

DR. LAURENCE L. ROBBINS: The barium enema was said to be negative. The only films that show the liver and the spleen are these. Neither appears enlarged.

DR. ADAMS: Is there any enlargement of the gall bladder?

DR. ROBBINS: No.

DR. ADAMS: What about the kidneys?

DR. ROBBINS: The left kidney is normal, and I think the right kidney is also normal.

DR. WILLIAM B. BREED: The spasm of the antrum is of no significance?

DR. ROBBINS: Only of suggestive value. We see pylorospasm occasionally in cases of acute cholecystitis.

DR. BREED: Was there pylorospasm in this case?

DR. ROBBINS: That would be determined chiefly on fluoroscopy. However, there is narrowing of the antrum on all the films; this is indicative of some spasm.

DR. ADAMS: The fundamental problem in this case is to decide whether the jaundice was due to intrahepatic disease or to biliary-tract obstruction. With a sixty-six-year-old man with progressive

painless jaundice, one thinks immediately of obstruction due to carcinoma of the pancreas. Yet we have very little evidence on which to establish such a diagnosis. There were no preliminary digestive symptoms, no weakness and no loss of weight, which one often sees early with carcinoma of the pancreas. What is more important, neither the liver nor the gall bladder was shown to be enlarged clinically or roentgenologically, and no pressure defect of the duodenum was observed roentgenologically. Furthermore, the brown color of the stool rules out complete block. The only evidence in favor of obstruction is provided by the van den Bergh test: when, as in this case, the direct value is as high as 70 per cent of the total value, an obstructive type of jaundice is indicated. However, *I always dislike basing a diagnosis on a single laboratory test when the clinical picture is not typical.* I am further confused by the fact that the patient is reported clinically to have been deeply jaundiced, whereas the van den Bergh reaction indicates at most only moderate jaundice.

If the case were one of obstructive jaundice, carcinoma of the head of the pancreas would be most likely. There is certainly nothing to suggest the other common cause of obstruction—stone in the common duct. A remote possibility that deserves brief mention is that the obstruction might have been due to extension of a slowly growing tumor of the right kidney. We have no direct evidence, to be sure, but the two attacks of hematuria cannot be entirely disregarded.

What have we on the other side of the question? This patient was presumably perfectly well until he developed a streptococcal infection of the throat. That the infection was a fairly severe one might be postulated on the basis of the fact that he was given sulfanilamide. Following this illness, he was never entirely well, and four weeks after its onset the jaundice appeared. So-called "catarrhal jaundice" is often preceded by a respiratory infection, but usually appears within a few days—not after four weeks. Despite the interval, however, I cannot convince myself that the jaundice was not related to the infection, and that when the patient entered the hospital he was suffering from intrahepatic disease. Leukocytosis is not seen in simple catarrhal jaundice; yet it is not inconsistent with a severer form of toxic or infectious hepatitis that is proceeding toward acute yellow atrophy. That this stage of yellow atrophy had not been reached, however, is indicated by the absence of fever and other serious systemic signs. Occasionally, one encounters acute cholangitis secondary to severe streptococcal or pneumococcal infection, but this is not likely in this case *because the patient was not sick enough, did not*

have a sufficiently elevated leukocyte count, and had no enlargement or tenderness of the liver. Could the jaundice have been related to the sulfanilamide? I doubt it, for if so, it would have appeared much sooner.

To summarize, there does not appear to be sufficient evidence on which to base a diagnosis, which is often true in cases of jaundice. As I said earlier, at first glance one would be suspicious of obstructive jaundice due most likely to carcinoma of the pancreas. But none of the expected or corroborative signs of biliary obstruction were present, and the illness started with a respiratory infection. Frankly, I am rather surprised that the surgeon was willing to explore so promptly. Had this patient been under my care on the medical service, I am certain—*unless there were other facts available that do not appear in the record—that I should have pursued a course of watchful waiting for a week or ten days, treating the patient for acute intrahepatic disease and following the clinical course, particularly the progress of the jaundice.* In the absence of any improvement, I should have recommended exploration, because of the impossibility of differentiating biliary obstruction and intrahepatic disease.

On the evidence available, my diagnosis is acute hepatitis following an acute upper respiratory infection.

DR. MALLORY: Could we have an opinion from the surgical side? Dr. Sweet, would you be inclined to explore this man?

DR. RICHARD H. SWEET: I do not know. From what I have heard this morning, I should be inclined to agree with Dr. Adams. I should have wanted a little more study, especially about the relation between the evidence of obstruction and the van den Bergh reaction. The fact that there was apparently a dark-brown stool on one occasion seems to be slightly inconsistent. I might have studied that situation a little more.

DR. ADAMS: Will the surgeon who operated on this man tell us why he operated so promptly?

DR. MALLORY: Unfortunately, he is not here.

CLINICAL DIAGNOSES

Adenocarcinoma of ampulla of Vater.
Pancreatitis.

DR. ADAMS'S DIAGNOSIS

Acute hepatitis.

ANATOMICAL DIAGNOSES

Papillary adenocarcinoma of ampulla of Vater.
Obstructive jaundice.

Operative wound: resection of duodenum and portion of head of pancreas, gastrojejunostomy and cholecystoduodenostomy.

Abscess of pancreas, with extension into retro-peritoneal tissues.

Intrahepatic cholangitis.

Arteriosclerosis, moderate: aortic and coronary

PATHOLOGICAL DISCUSSION

DR. MALLORY: The patient was explored, with a preoperative diagnosis of obstructive jaundice. At operation, a small mass could be felt in the duodenum in the region of the ampulla. The head of the pancreas felt normal. The common bile duct was somewhat dilated and contained bile. It was believed that tumor was unquestionably present, either in the head of the pancreas or in the duodenum, and it was decided to do a block dissection. Accordingly, the stomach was divided in the antral region, and the duodenum was cut just before the ligament of Treitz. The common duct was divided, the pancreas was resected about a third of the way back from the head, and the entire block of tissue was removed in one piece. When it was opened, a slightly papillary and very slightly ulcerated tumor was found in the wall of the duodenum surrounding the ampulla of Vater. On microscopic examination, it proved to be a well-differentiated carcinoma, evidently primary in the ampulla. There was one regional node that showed metastases. Following operation, the patient began to run a septic temperature, and from that time on failed rather rapidly, dying in about two weeks.

At autopsy, extensive necrosis was found in the head of the pancreas. A large abscess had burrowed from the pancreas down into the right gutter. There was likewise a cholangitis, and some degree of hepatitis. It would not be possible to say from the autopsy findings whether the cholangitis and hepatitis had been present before operation. At any rate, there was no established biliary cirrhosis, although there was considerable infection in the bile ducts of the liver.

CASE 28332

PRESENTATION OF CASE

A forty-one-year-old Syrian barber was admitted to the hospital because of recurrent attacks of vomiting.

The patient was well until five years before entry, when he suffered an illness lasting about ten days and characterized by nausea and vomiting. The night preceding the illness, the patient had eaten and drunk heavily. There was no fever, jaundice or other symptom. The trouble abated spontaneously, leaving the patient well until a year later, and again the year after that, when he experienced a similar illness, each period lasting ten days. Seven months before entry, the patient

had a fourth attack of nausea and vomiting, this time preceded by a month of anorexia and slight weakness. He visited a community hospital, but returned home after a few days, his trouble having stopped. Anorexia, fatigue and some nausea remained. After a month, the vomiting recurred, following a roentgenologic examination of the gastrointestinal tract. This examination showed a "filling defect at the pylorus." The patient entered another community hospital, where he was given gastric lavage and intravenous feedings. After a week, he stopped vomiting. He was placed on an ulcer diet, and improved readily. In the next five months, he steadily lost weight (about 25 pounds in all) and suffered considerable nausea, with occasional vomiting. At times he had mild diarrhea. Ten days before entry, a final attack of severe vomiting began, persisting until the day he came to the hospital.

About twenty years before entry, the patient had a soft sore on the penis, lasting several weeks. Ten years later he had gonorrhea, with a residual stricture of the urethra that caused him persistent difficulty in starting his stream.

The family history was irrelevant.

On admission, the patient appeared chronically ill, emaciated and dehydrated. The pupils were wide and irregular, and reacted poorly to light and only slightly better to accommodation. The fundi were normal. The heart and lungs were not remarkable. The liver edge was palpable on inspiration, but was smooth and not tender. The urinary bladder rose to two fingerbreadths below the umbilicus. The prostate was twice the normal size and symmetrical, without palpable nodules. The reflexes were equal and active. Vibration sense was present, but position sense was impaired.

The blood pressure was 130 systolic, 85 diastolic. The temperature was 99°F, the pulse 85, and the respirations 20.

Examination of the urine showed a ++ test for albumin, and a sediment with 20 white cells and rare red cells per high power field. The red-cell count was 7,600,000 with 14 gm. hemoglobin, and the white cell count 14,700 with 68 per cent polymorphonuclears, 29 per cent lymphocytes and 3 per cent monocytes. The blood Hinton reaction was positive. The serum protein was 4.8 gm. per 100 cc., with an albumin-globulin ratio of 1:3. The nonprotein nitrogen was 26 mg. per 100 cc., and the van den Bergh reaction was normal; the phosphorus was 2.4 mg. per 100 cc., the phosphatase 31 Bodansky units, and the prothrombin time 25 seconds. Three stools were guaiac negative. Gastric aspiration produced 125 cc. of greenish, guaiac-negative fluid. A lumbar puncture showed clear fluid under normal pressure, with a cell count of 16 lymphocytes, a total protein of 32 mg.

per 100 cc., a + ammonium sulfate ring test, a positive Wassermann reaction and a gold-sol curve of 4332211000.

Roentgenographic examination of the upper gastrointestinal tract showed thickening of the folds of the stomach, with ready opening of the pylorus. The duodenal cap was rather small, and there was some narrowing at the junction of the first and second portions of the duodenum. After barium passed into the duodenum, it extended into an apparently dilated common duct, cystic duct, gall bladder, major hepatic ducts and some minor intrahepatic branch ducts. The first portion of the duodenum then showed irregular filling defects and two or possibly three fine fistulous tracts passing from this part of the duodenum to the gall bladder (Fig. 1). In

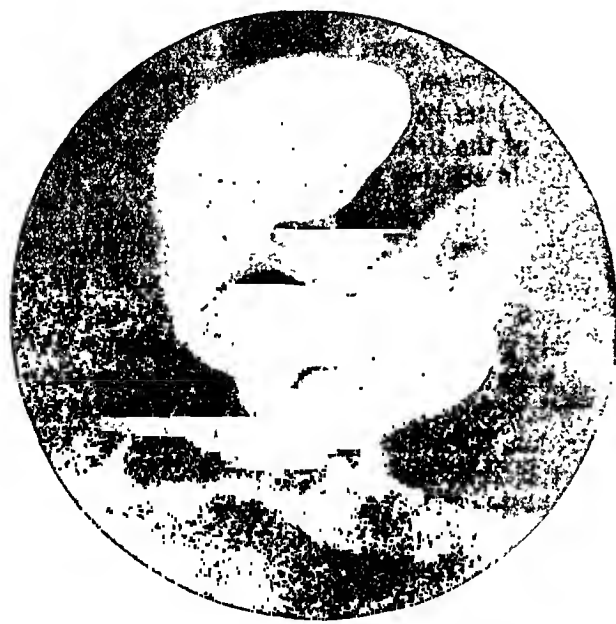


FIGURE 1.

This photograph shows barium filling of the gall bladder (upper left) through three small fistulas passing up from the deformed duodenal cap.

re-examination on the following day, the fistulous tracts failed to fill with barium.

The patient was given intravenous fluids, with resultant relief of dehydration and restoration of the red-cell count to normal. He took fluids well, but vomited several times, usually in large quantity. He had no pain until the night of the seventh hospital day, when he began to complain of cramping in the lower abdomen. At this time, the abdomen was soft, with loud peristaltic sounds. The temperature was 101°F. An enema produced good results and relieved symptoms temporarily. The next morning, the patient suddenly collapsed. When seen a few minutes later, he was unconscious and quite cyanotic, with a blood pressure

of 40 systolic, 0 diastolic. The pulse and respirations were but slightly elevated. Examination of the chest was negative. The abdomen was soft and silent, not distended. The patient was given intravenous fluids, and transfusions of both blood and plasma. He responded within half an hour. In the course of the day, he developed increasing distention, and complained intermittently of pain in the left lower quadrant. The temperature returned to normal. The next day, there was generalized abdominal tenderness, centering in the left lower quadrant.

The patient was given constant gastric suction and intravenous fluids. He became unconscious on the evening of the ninth hospital day, and died five hours later.

DIFFERENTIAL DIAGNOSES

DR. RICHARD H. SWEET: A few comments on certain aspects of the history are in order. "Seven months before entry, the patient had a fourth attack of nausea and vomiting, this time preceded by a month of anorexia and slight weakness." This suggests something different, a new train of symptoms.

This examination showed a "filling defect at the pylorus." One wonders if the patient was not beginning to suffer from an obstructing lesion, which produced the anorexia, fatigue and, perhaps, the nausea and the loss of weight and strength.

"The pupils were wide and irregular, and reacted poorly to light and only slightly better to accommodation"; this suggests Argyll-Robertson pupils.

"The urinary bladder rose to two fingerbreadths below the umbilicus." One begins to think seriously about tabes, and the spinal-fluid findings are confirmatory.

"The prostate was twice the normal size." That might have entered into the picture. The patient might have had obstruction of the urethra because of an enlarged prostate.

He had a fairly normal temperature and a reasonably normal differential count. One might assume that he was not suffering from an inflammatory process or an acute infection. If he had a carcinoma of the pylorus, one would expect to see blood in the stools.

"Gastric aspiration produced 125 cc. of greenish, guaiac-negative fluid." Once again, doubt arises regarding the correctness of the first impression that he might be suffering from carcinoma of the stomach.

May we see the x-ray films?

DR. LAURENCE L. ROBBINS: There is quite definite thickening of the folds of the stomach, but as nearly as I can make out, this is antrum and this

represents the duodenal cap. Here, of course, is the common duct filled with barium, and here must be the gall bladder, with the cystic duct visible in this region. These spot films demonstrate the fistulous tracts between the gall bladder and the first portion of the duodenum.

DR. SWEET: Do you think the biliary system filled through the fistulas or by regurgitation through the common duct?

DR. ROBBINS: Not having seen it fluoroscopically, I do not know, but the appearance of the common duct in the distal portion is not what one sees with retrograde filling. I should guess that it had filled through the fistulas.

DR. SWEET: So that we have the problem in this case of deciding what was the cause of the fistulas. In surgical practice, one encounters relatively few causes of that condition. The commonest is ulceration from the gall bladder into the duodenum, with necrosis of a portion of the gall bladder, usually attributed to pressure from a stone in association with infection. Most of the cases of gallstone ileus result from the passage of a large stone directly from the gall bladder through this wall of the duodenum, down into the intestinal tract. This causes a large fistulous opening. Carcinoma of the gall bladder, in my experience, rarely leads to a condition such as this. Here is a fairly normal-looking gall-bladder shadow. There is a well-defined common-duct shadow, and one might exclude carcinoma arising in the region of the cystic duct. Carcinoma of the duodenum is exceedingly rare. The few that I have seen were in the third portion.

Could the fistula have been due to a syphilitic lesion? Are gummas seen in this region? If so, would a gumma produce ulceration through the duodenum and into the gall bladder? I doubt it. The patient was a Syrian. Did he have echinococcal disease? There is no evidence for it, at least no x-ray evidence, and no mention of enlargement of the liver. Echinococcal cysts that obstruct the common duct from the passage of daughter cysts down the duct are occasionally encountered. In this case, however, there was apparently no common-duct obstruction, although one cannot be sure because one does not actually see that the barium went out into the duodenum through the common duct. There was no jaundice. According to the history, I believe I can exclude echinococcal disease. No echinococcus fixation test was done.

Since I cannot answer the question about the relation of syphilis, I shall go on with this lengthy and puzzling story. I do not know why the patient died or what he had. I believe he must have had peritonitis, but how he developed it, I am sure I cannot tell. I should think that, if he had had

leakage from one of the fistulas in the right upper quadrant, the tenderness would have been maximal there or in the right lower quadrant instead of the left.

What conditions give rise to peritonitis in the left lower quadrant? Of course, the organs that one finds there—the sigmoid and so forth—may be the cause. Conditions arising in the upper abdomen may include some retroperitoneal hemorrhage or evacuation of an abscess retroperitoneally from the pancreas. Fluid arising in the upper abdomen from perforation of the stomach, duodenum, gall bladder or common duct usually passes down on the right side. Of course, I cannot tell; I did not see the patient. It may have come down on the right and gone over to the left side, but I get the impression from this—whatever the sudden episode was—that he had something producing the maximum of reaction in the left lower quadrant. It is fair to assume that the patient had as a final episode a generalized peritonitis unless there was something else, like intra-abdominal hemorrhage, which one could not tell anything about from this record. The case is exceedingly puzzling. To summarize, I believe the patient had some peculiar lesion in the duodenum or gall bladder, which I suppose was the origin of the sudden abdominal catastrophe that was the cause of death.

DR. TRACY B. MALLORY: Are there any questions or suggestions?

DR. FULLER ALBRIGHT: How about a ruptured aneurysm?

DR. MALLORY: Where?

DR. ALBRIGHT: I do not know.

DR. SWEET: That is what I meant when I said "intra-abdominal hemorrhage."

DR. MALLORY: Dr. Dieuaide, how much of a role would you consider syphilis to have played in this process?

DR. FRANCIS R. DIEUAIDE: I think it probably played none. Gummas may occur in that region perfectly well, but are unusual. I do not believe, however, that a syphilitic process in this region would be likely to be associated with fistulas. The fistulous nature of the lesion is an important clue. A gummatous process here would be an adhesive, more or less solid, mass. Accordingly, I should abandon syphilis as the explanation of the lesion, although the patient certainly had central-nervous-system syphilis. I should consider it meningovascular rather than tabetic. I do not believe an aneurysm could be used to explain the whole story, although a ruptured aneurysm could be the explanation of the terminal episode.

DR. ALBRIGHT: I believe the fistula was due to stone.

nurses-aide committee, a Red Cross nursing consultant may visit the hospital, or information may be obtained from the state nursing council or the state nurse-examining board.

Each nurses' aide agrees to give one hundred and fifty hours of service in each calendar year, preferably within a three-month period. In case of need for war service, nurses' aides must be prepared to serve locally in the emergency for as long as they are needed.

The Office of Civilian Defense has asked its regional-office representatives to work out plans for stimulating the recruitment of nurses' aides to provide the needed strength to meet war demands. These plans are to be put into effect through the officially constituted authorities, including state and local chiefs of emergency medical service, their nurse deputies, local Red Cross chapters and local civilian-defense volunteer offices.

Without the assistance of large numbers of nurses' aides to supplement the registered nurses, many hospitals report that they would be unable to provide adequate nursing services. If coastal and industrial cities are subjected to enemy attack, the need for nurses' aides will be greatly accentuated. The goal of 100,000 trained nurses' aides must be reached, the Medical Division declares. In no other branch of service can women be of greater value to the war effort.

CORRESPONDENCE

MEDICAL ADVISORY COMMITTEE FOR INDUSTRIAL ACCIDENT BOARD

To the Editor: When the Massachusetts Workmen's Compensation Act became a law, a committee representing the medical profession met and discussed the important medical aspects of such an act; at the meeting, this committee established a few fundamental policies which were adopted by the Industrial Accident Board and became the backbone of the compensation law. These policies have developed and grown as a result of the continued advice and study by representatives of the medical profession as a whole.

I believe that the success of the Industrial Accident Board in Massachusetts, and its high standing in other states, is due in a considerable degree to the assistance we have received from many members of the medical profession recognized as specialists in their respective lines of work.

It is the desire of the Board to continue this policy and, although many are well qualified throughout the Commonwealth to serve the Board in an advisory capacity, it is expedient and desirable that such a committee be located near the offices of the Board.

I am, therefore, pleased to announce the appointment of the Medical Advisory Committee as follows:

Dr. Cadis Phipps, chairman, 587 Beacon Street, Boston. Director, First and Third Medical Services, and physician-in-chief, Third Medical Service, Boston City Hospital; professor of medicine and head of Department of Medicine, Tufts College Medical School; diplomate, American Board of Medicine.

Dr. William E. Browne, secretary, 587 Beacon Street, Boston. Associate, Surgical Staff, Beth Israel Hospital; surgeon-in-chief, Second Surgical Service, Carney Hospital; clinical professor of surgery, Tufts College Medical School; fellow, American College of Surgeons; diplomate, American Board of Surgery.

Dr. Donald Munro, Boston City Hospital, Boston. Surgeon-in-chief for neurological surgery, Boston City

Hospital; associate professor of neurological surgery, Boston University School of Medicine; assistant professor of neurological surgery, Harvard Medical School; member, American Neurological Association, New England Surgical Society and Society of Neurological Surgery; fellow, American College of Surgeons; diplomate, American Board of Neurological Surgery and American Board of Surgery.

Dr. William A. Rogers, 266 Beacon Street, Boston. Instructor in orthopedic surgery, Harvard Medical School; member, American Orthopedic Association; fellow, American College of Surgeons; diplomate, American Board of Orthopaedic Surgery.

Dr. John G. Downing, 520 Commonwealth Avenue, Boston. Assistant dermatologist, Boston City Hospital; assistant professor of dermatology, Tufts College Medical School; consultant, United States Public Health Service; member, Boston Health Department, American Academy of Dermatology and Syphilology (vice-president), American Association of Industrial Physicians and Surgeons, American Dermatological Association, Society of Investigative Dermatology and New England Dermatological Society; diplomate, American Board of Dermatology and Syphilology.

Dr. Ariel W. George, 43 Bay State Road, Boston. Member, American Roentgen Ray Society, British Institute of Radiology, New England Roentgen Ray Society and Radiology Society of North America; diplomate, American Board of Radiology.

Dr. Timothy Leary, 43 Bay State Road, Boston. Medical examiner, Suffolk County; professor of pathology, emeritus, Tufts College Medical School; lecturer in legal medicine, Harvard Medical School.

These men are recognized as specialists by members of their profession and, I believe, will render invaluable service to the Commonwealth.

EMMA S. TOUSANT, *Chairman*
Industrial Accident Board

State House
Boston

DEATH RATE IN INFANCY AND CHILDHOOD

To the Editor: The editorial that appeared in the July 9 issue of the *Journal* on the subject, "Death Rate in Infancy and Childhood," has been the subject of discussion among the members of our division staff.

We have read the article by Dublin and Spiegelman therein quoted. The three years chosen for the study include the very last of the years (1937) when the Massachusetts' infant mortality rate was above 40. In the remaining two years, 1938 and 1939, the rate was below 40, and it has continued to decrease. The rates for these years are as follows: 1937, 43.8; 1938, 39.1; 1939, 37.4; 1940, 37.5; and 1941, 35.3.

We fully appreciate the problems presented by the unusual conditions of the present and the future and shall do our utmost to "hold fast to the ground that has already been gained." To that end we feel sure we may call on the continued co-operation of the medical profession in Massachusetts.

FLORENCE L. MCKAY, M.D., *Assistant Director*
Division of Child Hygiene

73 Tremont Street
Boston

WILLIAM HENRY WELCH

To the Editor: The excellent editorial on William Henry Welch in the July 23 issue of the *Journal* reminds one of the esteem shown him by his associates. I recall walking the hospital wards with Dr Osler in the early days of Hopkins. Discussing a medical problem, Dr Osler inquired, 'Well, what does the king of all pathologists say to this?'

A present-day visitor to the school is struck by the inscription across the façade of the Anatomical Building, 'The Woman's Fund Memorial Building 1894'. This marks an end to the long struggle to raise sufficient money to warrant opening the school. A group of women with the timely help of Miss Mary Garrett, offered the University a fund of half a million dollars on the conditions that women should be admitted on the same terms as men and that the entrance requirements should be on a university level.

Some years later, Dr Welch, speaking at the annual meeting of the Association of American Universities on 'Women in Medicine,' said 'The faculty of Hopkins deserves little credit for the success of the school. Only Osler, Kelly and Hurd signed a letter of acceptance to the proposition of the women, the rest of us were frankly skeptical about the experiment of coeducation. Now, after the actual experience, I am sure that I report my colleagues correctly that we would unanimously vote to continue coeducation in the medical school. That medical education belongs to a university and that women are to participate in the intellectual aspect of medicine mark an epoch in American medicine.'

Among the treasures also to be seen by the visitor, is the Sargent group of the Great Four. Of Dr Welch sitting in front, Dr Osler once remarked, 'One sees his strength as an aura.'

SARAH ELLEN PALMER

186 Commonwealth Avenue
Boston

REPORT OF MEETING

HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on April 14, with Dr C. Sidney Burwell presiding. There was a case presentation by the medical service.

A sixty-four year old man was first admitted in 1940 because of asthmatic breathing of eighteen months' duration. Physical examination was essentially negative except for the liver, which could be palpated 4 cm. below the right costal margin. There were no significantly enlarged lymph nodes, and the spleen was apparently normal. The red-cell count was 4,800,000, and the white cell count 11,000 with a normal blood smear. In December 1941, the patient returned because of a loss of 15 pounds in weight, weakness and gaseous eructations. Physical examination revealed an enlarged liver and a palpable mass in the left upper quadrant. This finding was confirmed by x-ray studies as the spleen, no gastrointestinal defects were demonstrable. On admission to the medical service two weeks later, the patient was found to have a considerable amount of fluid in the left pleural cavity and generalized lymphadenopathy, as well as hepatomegaly and splenomegaly. The white cell count was 126,000 with 93 per cent large lymphocytic cells. One thousand cubic centimeters of fluid was removed from the left pleural cavity. After three spray treatments of x-rays of

50 r each, directed from the clun to the knees, there was within twelve days a decrease in the white-cell count to 13,000. The percentage of lymphocytes remained about the same. Two months later, there was great subjective improvement, and the leukocyte count was 5000, three months later, the white cell count was 7000, with 50 per cent polymorphonuclear neutrophils.

In the discussion, Dr William Dameshek questioned whether regional roentgen ray therapy is not better for decreasing the white cell count and increasing the red cell count. Dr M. C. Sosman stated that much better results are obtained with spray therapy using small dosage. There is apparently less systemic reaction, and the erythrocyte count rises more gradually and is longer sustained. Regional roentgen ray therapy is now used by him only for the alleviation of subjective local signs.

The speaker of the evening was Dr Louis Hamman of Johns Hopkins University School of Medicine, who discussed 'The Diagnosis of Leukemia.' This disease is now better known for its bizarre onset in many cases than was formerly noted. A patient may present anything from a peridental abscess or tachycardia to change of bowel or urinary habits. Any of the bodily systems may supply the initial symptom. There is one group in which the early blood picture fails to reflect the true state of affairs, and these conditions are therefore particularly difficult to detect. Another recent development that complicates the diagnosis of leukemia is the recognition of so-called 'leukemoid reactions' which result in almost identical hemograms. These may be the result of irritation or stimulation of the bone marrow, such as that in osteomyelitis and other infections, complicated fractures, metastatic cancer completely replacing the active marrow and leading to the establishment of other foci of hematopoiesis, Hodgkin's disease and benzol poisoning which may eventually be exactly the same and has been suggested by some as an etiologic factor. A marrow response to regeneration, as in the acute familial hemolytic jaundice, severe hemorrhage, agranulocytosis and severe infections, and myelophthisis, a condition in which ectopic foci of hematopoiesis arise in the primitive blood-forming organs when the marrow is inadequate because of such conditions as osteosclerosis and fibrosis, extensive tumors and the late stages of increased demands on the regenerative system. In the first group the leukocyte count may be very high and there is usually marked eosinophilia and immaturity of the leukocytes. In the second group, there is only moderate leukocytosis and immaturity and less eosinophilia. In the last group the leukocyte count may be anything, but there is often increased immaturity of cells, whereas eosinophilia is not common.

In the diagnosis of leukemia one should be careful not to include any of the above conditions, especially those with a favorable prognosis for there is nothing worse than to have a family prepared for an inevitable death that fails to materialize. When leukocytosis and immature white cells are present the diagnosis of leukemia is not difficult. But this cannot be said of the subleukemic, leukemic and leukopenic stages. In true leukemia, there is always—except perhaps during remissions—some degree of anemia, which may be pronounced too severe with an increase of normoblasts. The platelets are invariably very low. Immaturity of leukocytes occurs in about 90 per cent of the cases, and the cells are often atypical. Various cell families may sometimes be differentiated only by mobility tests.

Dr Hamman cited some case histories to indicate the

problems involved. In one, a seventy-five-year-old man had pericarditis with effusion and no demonstrable blood change for several months. Therefore, a patient may have leukemia for some time without blood changes, and certain diseases may terminally become leukemia. Another case of the same type had symptoms without recognizable changes of the hemogram for four months: a middle-aged woman had recurring fever, with two positive agglutination tests for *Brucella mellitensis*, and tubercle bacilli were cultured from a lymph node before the blood picture became that of leukemia. At autopsy, all organs revealed typical findings of leukemia, but of the more acute type. However, a review of blood smears revealed that there was an early anemia and granulopenia and that the 90 per cent of the "lymphocytes" were in reality myelocytes and myeloblasts. Subsequent smears showed an accentuation of all features of a true leukemia. Clinically, it was concluded that the patient had had this disease from the beginning, with intercurrent Malta fever and localized tuberculosis, but the pathologist stated that the course could not have been of seven months' duration. This raises the question whether leukemia may result from stimulation by poisons, infections and so forth. Malta fever is known to occasion leukemoid reactions.

Another case was that of a fifty-nine-year-old man who was suspected of having a duodenal ulcer but had roentgenologic evidence of it for only a short while. On developing signs and symptoms of a perforation, the patient was subjected to an operation, but no ulcer was found. During and after the convalescence, the pain continued and became severer until it was almost unbearable. Roentgenograms revealed what appeared to be multiple bone metastases, and some slight relief resulted from irradiation therapy. On admission, the blood picture was normal, but the erythrocyte count soon fell, whereas that of the leukocytes rose and more immaturity of these cells became apparent in blood smears. Autopsy a few weeks later revealed characteristic leukemia, the cause of sudden death being a subarachnoid hemorrhage—not a rare occurrence.

In conclusion, Dr. Hamman stated that leukemia may be present for some time with signs and symptoms but no characteristic blood changes, just as well as the opposite. In children, it is likely to simulate acute infections, whereas in adults chronic infection and cancer are usually suspected.

The discussion was opened by Dr. E. A. Stead, Jr., who emphasized the fact that myelocytes are frequently called lymphocytes in unknown smears. Dr. Chester S. Keefer asked whether leukemia might not be caused by multiple small doses of irradiation. Dr. Louis K. Diamond pointed out the difficulties in children, in whom infection so often elicits a bizarre blood response. More than 50 per cent of his leukemic patients were in the leukopenic stage on admission, and biopsy is, therefore, often used. Signs and symptoms of rheumatic fever are fairly common and are always associated at the onset with relatively low leukocyte counts. The importance of thrombocytopenia as a diagnostic aid was emphasized.

In answer to a question by Dr. Sosman on how best to treat early cases when the total white-cell count is essentially normal, but the percentage of young forms is high, Dr. Hamman stated that irradiation therapy may actually be harmful and should be reserved for the onset of symptoms. Temporarily, supportive treatment should be employed.

BOOK REVIEW

Behind the Mask of Medicine. By Miles Atkinson, M.R.C.S., L.R.C.P. 8°, cloth, 348 pp. New York: Charles Scribner's Sons, 1941. \$3.00.

This book, like those of "The Doctor Looks at —" sort, is designed for lay consumption. It contains some history and considerable philosophising concerning the relation of the patient to the doctor, medical economics and the present and potential status of medical practice.

Dr. Atkinson is fluent, sometimes thought provoking, and not infrequently amusing. But the title of the book, connoting as it must in some minds something camouflaged or deliberately concealed, is inappropriate and unfortunate. Moreover, the author is sometimes just a little too glib, a shade too cocksure. His insouciance is the more conspicuous in the face of certain careless errors and misleading implications. It is not true, for example, that vitamin E is "the latest of the vitamin discoveries." It is not true that a blood count is "the only laboratory procedure which is absolute." The statement that "some small boys keep for preference their testicles high up out of the way where they do not develop properly" will not have much meaning for most readers. Furthermore, Christopher Wren is hardly to be bracketed with Francis Bacon and Sir Isaac Newton as a motivating force in seventeenth-century science.

This is not meant for captious criticism; it is simply that carelessness about minutiae tends, even with some injustice, perhaps, to break down an author's credit with those in the know. Dr. Atkinson has some chapters that are quite free from either factual blemishes or "wisecracks"; the chapter on the plight of the hospitals deserves every doctor's, every hospital director's and every trustee's reading. That the chapters on socialized medicine and the future will provoke controversy is inevitable,—those are controversial subjects,—but nothing against the author.

All in all, it is a book to be read with a certain added salinity of the reader's seasoning—a good dose of salt, in spots. If one knows how to add it, well and good; if he has any doubts how, it would be wiser to let it alone.

NOTICES

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, AUGUST 16

MONDAY, AUGUST 17

12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, AUGUST 18

12:15-1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

WEDNESDAY, AUGUST 19

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

SEPTEMBER 9-12. American Congress of Physical Therapy. Page x, issue of May 14.

SEPTEMBER 29, 30 AND OCTOBER 1. Connecticut Clinical Congress. Yale Law School Building, New Haven, Connecticut.

SEPTEMBER 30-OCTOBER 10. Conference and Course in Legal Medicine. Page ix, issue of July 23.

OCTOBER 12-23. 1942 Graduate Fortnight. New York Academy of Medicine. Page xi, issue of May 21.

OCTOBER 14-17. American Academy of Physical Medicine. Hotel Statler, Boston.

OCTOBER 19-23. 1942 Clinical Congress of the American College of Surgeons. Page ix, issue of February 5.

(Notices continued on page ix)

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SURGICAL TREATMENT OF SEVERE ORCHITIS IN MUMPS*

CONRAD WESSELHOEFT, MD,† AND SAMUEL N. VOSE, MD‡

BOSTON

THE early surgical treatment of severe orchitis of mumps accomplishes prompt relief of pain and saves the testicle from subsequent atrophy. The operation must be done before the testicular tissue has undergone pressure necrosis, but should be reserved for cases in which the severity of the symptoms warrants such interference.

In 1864, Henry Smith¹ advised multiple punctures of the tunica albuginea for orchitis; he stated that this operation had been in vogue in Paris for at least two years. One finds references to this work in the literature on mumps, but the orchitis so treated was of gonorrheal origin. Comby,² in his book on mumps published in 1893, makes no mention of any surgical treatment of orchitis. Schottmüller,³ in 1904, advised incision through the tunica vaginalis for release of the hydrocele fluid in mumps orchitis. In 1912, G. G. Smith⁴ treated 2 patients with mumps orchitis by incising the tunica albuginea, and in 1920, Billenger and Elder⁵ reported on 3 patients so treated.

Edema is characteristic of the pathology of an invasion of gland tissue by the mumps virus. The dense fibrous layer covering the testicle offers resistance to this swelling. If the edema develops rapidly, the internal pressure causes intense pain, often associated with backache. Repeated chills, with high fever, nausea, vomiting and even delirium, may take place. The pain may be so excruciating that $\frac{1}{2}$ gr of morphine fails to give relief, and so tender is the part that the patient objects to the most gentle examination. This situation may develop rapidly in fulminating cases, in which the testicle swells rapidly and hydrocele fluid forms. The scrotum becomes

markedly edematous and bluish red. In other cases, the testicle may gradually reach double its normal size in forty-eight hours, with only moderate discomfort, slight tenderness, no edema of the scrotum and only a moderate fever. It may subside gradually, when no surgical interference is necessary, or it may suddenly develop into the fulminating picture described above.

Although mumps is manifested by a parotitis in the vast majority of cases, it is well to keep in mind that the parotids may show no swelling, and that the submaxillary and sublingual glands may take the brunt of the attack. Furthermore, the involvement of the salivary glands may follow other manifestations of the disease. Thus, an orchitis, a pancreatitis or an encephalitis may precede, accompany or follow the parotitis. Finally, the only manifestation of mumps may be in one of these organs remote from the salivary glands. Here, the diagnosis is based on the circumstantial evidence of exposure, the incubation period of approximately eighteen days and the course pursued. In 1920, Wesselhoeft⁶ collected from the literature 30 cases of primary orchitis and 64 cases in which orchitis occurred without involvement of the salivary glands. Since then, several more have been reported. During epidemics, such cases crop out, and to add to the difficulty, they may occur in patients who have had mumps previously. However, one attack of the disease, even though it affects only one salivary gland, usually conveys a lasting immunity.^{7, 8}

Orchitis very rarely occurs before the age of puberty, but such cases have been recorded. At and above that age, its incidence in mumps is 18 per cent. Collected reports from the literature indicate that under epidemic conditions both testicles are likely to be involved in 1 out of 6 cases.⁶

In the follow-up examinations of 347 cases atrophy was revealed in 190, or 54.7 per cent.⁶ Sterility as a result of atrophy is actually rare. In

*Presented at a meeting of the New England Section, American Urologic Association, Boston, April 23, 1942.

From the Haynes Memorial Massachusetts Memorial Hospitals.

†Clinical professor of communicable diseases, Harvard Medical School; associate professor of theory and practice, Boston University School of Medicine; physician in chief, Haynes Memorial Massachusetts Memorial Hospitals.

‡Associate professor of genitourinary surgery, Boston University School of Medicine; surgeon in chief, Genitourinary Department, Massachusetts Memorial Hospitals.

the unilateral cases, the unaffected testicle serves adequately for procreation. In the bilateral cases, enough undamaged tubules remain to supply spermatozoa, but probably not in the usual abundance, and thus reduce the chances of conception to an indeterminable degree. Sterility is not to be confused with impotence. As pointed out by Stengel,⁹ sterility implies the lack of sufficient sex cells, whereas impotence refers to the inability to complete the sexual act. Fear of sterility after mumps orchitis sometimes leads to a mental complex that may promote impotence.

A description by Wolbach of the pathology of mumps orchitis is incorporated in the paper by G. G. Smith.⁴ In the biopsy specimen, it was found that the process did not affect the testicular tissue uniformly. Some groups of seminiferous tubules were completely destroyed. The interlobular connective tissue throughout was edematous, and between the tubules there were fibrin, small areas of hemorrhage, and many polymorphonuclear and endothelial leukocytes. Manca¹⁰ subsequently confirmed these findings in an autopsy specimen. The pathology of the parotitis in the experimental disease in monkeys has been described by Johnson and Goodpasture,¹¹ who found edematous swelling of the gland with pin-point hemorrhages and destructive changes through the parenchyma, including disintegration of the acinar cells and the presence of cytoplasmic inclusions. There was an infiltration of mononuclear phagocytes, and later of lymphocytes, into the necrotic areas and about the ducts. The authors found that healing took place through removal of the debris and regeneration of acinar epithelium, which restored the gland without scarring. In these two descriptions, there is a contrast that is of importance to the prognosis. Wolbach described a well-advanced orchitis in which the inflammation had called forth polymorphonuclear cells. In severe orchitis, the blood counts tend to shift from a lymphocytosis to a polymorphonuclear leukocytosis. This shift in the blood picture is comparatively rare in parotitis, involvement of the submaxillary glands, pancreatitis, encephalitis and oöphoritis. The reason for this rise in neutrophils seems to be a true pressure necrosis in the testicle, in addition to the benign and reparable inflammatory process seen in other organs. Furthermore, in no other gland does mumps invasion result in atrophy, with the possible exception of the prostate.¹²

The pathology in a totally atrophied testicle has been described by Stolz.¹³ The resistance of the tunica albuginea appears to be responsible for the severe pain and the pressure necrosis that leads to subsequent testicular atrophy.

The virus of mumps may invade the seminiferous tubules of the testicle, the epididymis and the vas deferens in varying degrees of severity, either simultaneously or separately. Moreover, in rare cases, the prostate and the seminal vesicles may also be involved.

Schottmüller³ recommended incision through the wall of the scrotum for the purpose of releasing the hydrocele fluid. This operation, however, did not relieve the pressure necrosis going on within the testicle, and therefore accomplished little or nothing. In our experience, hydrocele fluid increases more rapidly from an epididymitis than from an orchitis. However, if either of these conditions exists in a severe form, the other organ also becomes involved to a certain degree. The epididymitis, which is relatively less painful than that caused by gonococcal infection, is as self-limited as the swelling of the parotid. As the inflammation in the epididymis diminishes, the hydrocele recedes spontaneously. The only possible value, then, of an incision through the scrotum is to expose the testicle and thus to determine the situation more accurately, especially when the diagnosis is in doubt. In primary cases, the question of differentiation from an early torsion of the testicle may arise; therefore, a view of the testicle may be desirable.

At the onset of orchitis, the scrotal wall is thin, so that one can easily palpate the testicle and any enlargement of the epididymis. If the testicle does not yield to pressure, presents a stonelike hardness and is very tender, it is wise to operate without further delay. As the condition progresses into the severe stage, the actual size and firmness of the testicle become more obscured by the edema of the scrotum and the accumulation of hydrocele fluid.

An incision through the scrotum, which in these cases may be 1 cm. thick from edema, causes a spurt of yellow hydrocele fluid. This spurt may rise like a fountain toward the face of the operator, particularly if a small nick is made in the tunica vaginalis. The incision is enlarged with scissors to about 3 cm., thus exposing the surface of the testicle to view. There is no necessity of delivering the testicle as done by Smith⁴ and Ballenger and Elder.⁵ It may be turned within the scrotum to demonstrate the condition of the epididymis. In severe cases, the tunica presents a surface that does not yield to pressure and may be studded with small petechiae. The tunica albuginea is incised longitudinally to a length of 1.5 cm. The internal pressure may cause the testicular tissue to protrude through the incision. The greater the tension, the less the bleeding. Care is taken to avoid any outwardly visible blood vessel, and

small spurs may be secured by fine ligatures. Another incision, crosswise to the first but beside it, may be made to relieve tension in both directions. The scrotal incision is then stitched with silk, a small rubber-tissue drain or simply an open end of the wound being left to afford an exit for the profuse drainage that follows. The dressing should be secured by a T bandage, with two lines coming up over the groins. This dressing should be changed within two hours, and at frequent intervals through the first twenty-four or forty-eight hours, or as indicated by the amount of drainage.

Nitrous oxide and oxygen is the anesthetic of choice. We attempted to use local anesthesia in one case but without success, because the operation was much too painful. This was the only patient who expressed dissatisfaction with the operation at the follow-up examination. In another

On the follow-up examinations six months and one year later, this case showed some atrophy to have taken place, the testicle being noticeably smaller than the unaffected one; the scar was barely visible in the folds of the scrotum. G. G. Smith⁴ did not report on the follow-up of his 2 cases. Ballenger and Elder⁵ incised the tunica albuginea in 3 cases, and on the follow-up examinations twenty months to three years later, there was no evidence of atrophy.

Twelve patients with severe mumps orchitis were operated on at the Haynes Memorial Hospital (Table 1). Nine of these were followed up six months and one year later. In only 1 of the 9, the patient described above as being operated on late, was there any observable atrophy of the testicle when compared with the unaffected one. In a case followed at a boarding-school infirmary,

TABLE 1. Summary of Results of Treatment of Mumps Orchitis.

TYPE OF CASE	TOTAL NO OF CASES	TESTICLES INVOLVED	NO OF CASES FOLLOWED	TESTICLES WITH ATROPHY	TESTICLES WITHOUT ATROPHY
Severe (operation) . . .	13	14	10	1*	10
Mild (no operation) . . .	14	17	10	0	13
Totals	27	31	20	1	23

*Late operation

case, we used intravenous Pentothal Sodium, but this patient had a temperature of 103°F. at the time and squirmed about during the operation, although entirely unconscious. Furthermore, he remained in a deep sleep for two hours. With nitrous oxide and oxygen, the patient comes out of the anesthetic immediately after the operation. It is surprising how promptly the tenderness of the testicle subsides. While the first dressing is being changed, the incised testicle may be gently palpated without causing undue pain, whereas prior to the operation even the gentlest possible handling is barely tolerated.

There is an immediate feeling of relief after the operation. The temperature drops sharply. One of our patients with a temperature of 105°F. and a mild delirium at the time of the operation was mentally clear half an hour later. The temperature fell to 100°F. in four hours, and an uneventful recovery followed.

The stitches in the scrotum should be left in for one week, since there is a tendency for the wound to gape if they are removed earlier. When the operation is done within forty-eight hours of the onset, the swollen testicle may go down to almost normal size within a week, but more frequently this takes ten days to two weeks. One patient who was operated on late but had high fever still had an enlarged testicle after a month.

the second testicle became involved after the operation on the first; no atrophy took place. Thus, ten testicles were operated on early, with no subsequent atrophy, and one was operated on late, with subsequent partial atrophy.

With the exception of 1 patient operated on in 1929, all occurred in the years 1936-1941 inclusive. During this period, there were 10 cases of mild mumps orchitis at the Haynes Memorial Hospital. Four other mild cases were followed outside the hospital. These patients were not operated on. Follow-up examinations in 10 of these 14 cases revealed no atrophy. The absence of any evidence of atrophy after these mild cases is not in accord with an assertion by Stolz,¹³ based on reports of other observers, that the intensity of the inflammation during the orchitis is not a reliable indication of the amount of atrophy likely to ensue.

We have stressed the rapid fall in the temperature following operation. This statement needs qualification because the involvement of another organ may retard the fall in the temperature or subsequently cause a sharp rise. In 1 case, the second testicle became severely involved and was operated on two days after the first operation. Both testicles were normal in size at the follow-up examination. In 2 severe cases that came to operation, there was an accompanying encephalitis. In 2 of the mild cases

without operation, an encephalitis was the predominant complication. In 1 of these, the temperature rose abruptly to 107°F., accompanied by delirium, when the orchitis was superimposed on the encephalitis, but the testicle was never seriously threatened, and the temperature fell rapidly throughout the night. Aside from a lumbar puncture, there was no surgical interference, and no atrophy of the testicle followed. In 1 case, there was well-marked tenderness over the region of the pancreas, and the temperature was elevated.

The value of heat, cold and other applications, as well as morphine, is, in our opinion, beside the point in severe orchitis, as is any acute condition in which surgery is indicated. The use of convalescent serum is as illogical as it is ineffective. Whether the use of this serum in a case of mumps will prevent orchitis is a debatable question,¹⁴ and outside the scope of this paper. However, there is no doubt that convalescent serum is a valuable preventive against mumps when used soon after exposure.¹⁴

SUMMARY

The rationale of incising the tunica albuginea in severe orchitis is somewhat comparable to that of paracentesis of a bulging, painful drumhead in otitis media. The operation must be done sufficiently early to avoid pressure necrosis in the testicle. It is useless to operate when the process is already on the wane. Early operation relieves pain, reduces the fever and avoids atrophy. It is not indicated in mild cases or those in which an epididymitis predominates. An enlarged, hard, tender testicle, with chills and fever, constitutes the indication for surgical interference. Nitrous oxide and

oxygen is the anesthetic of choice. A rise in temperature after operation signifies an invasion of the virus in some other organ.

The end results of 9 hospital cases and 1 operated on elsewhere are presented. Moderate atrophy took place in the case operated on too late. In the others, there was immediate relief, and no atrophy was apparent at follow-up examinations. Fourteen cases of mild orchitis were observed during this period. The patients were not operated on. A follow-up examination on 10 of these revealed no atrophy. The expected incidence of atrophy after mumps orchitis without surgical interference is 54.7 per cent. Our experience suggests that atrophy occurs only after severe cases, and that by an early operation in such cases atrophy can be avoided.

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ECLAMPSIA

KENNETH W. SEWALL, M.D.*

BOSTON

THE purpose of this paper is to review some aspects of eclampsia and to present additional statistics.

ETIOLOGY

The cause of eclampsia remains unknown, in spite of many theories.

Placental infarcts have frequently been discussed as a cause of eclampsia. Recently, Hunt and his associates¹ suggested that placental infarcts and degenerating placental tissue liberate autolysates, which, if massive or if renal function is poor, produce severe late toxemia or eclampsia. Patterson et al.² caused acute placental infarctions, convulsions and death at term in rabbits by total thyroidectomy at the end of the first trimester of pregnancy. They believe that hypercholesterolemia of the fetus resulted in arterial disease, which accompanied fetal hypometabolism, and that placental infarctions and convulsions were due to split-protein products from the infarcted placenta.

Bartholomew and Kracke³ studied a thousand placentas and found acute infarcts in all those from patients who had pre-eclampsia or eclampsia. In their opinion, the infarcts are due to cholesterol-induced arterial disease and the eclampsia to the absorption of split-protein products from the infarcted area. They produced convulsions and death in guinea pigs by the injection of placental decomposition products.

Peters et al.⁴ found that 41, or 13 per cent, in a series of 320 patients with toxemia had had pyelitis or pyelonephritis, which, according to these authors, led to toxemia by producing renal damage and diminishing renal function. However, Mussey and Lovelady,⁵ in a series of 163 patients with pre-eclamptic toxemia or eclampsia, found 6 or 7 who showed symptoms of pyelitis in the puerperium. None gave a history of pyelitis before the first pregnancy, and among 117 cases of pyelitis of pregnancy, 3 patients developed acute hypertensive eclampsia and 1 died of an inflammatory kidney lesion. Prather and Sewall,⁶ studying 72 patients with pyelonephritis during pregnancy who returned to the hospital with a subsequent pregnancy, found that 13 per cent had toxemia. They point out that 10 per cent of all pregnant women have toxemia.

Strauss⁷ observes that 80 per cent of the women said to have toxemia actually have chronic vascular or renal disease before and after the gravid state, and that another 5 per cent have such disease in

acute form. The remaining 15 per cent have toxemia and, under proper care, will have normal succeeding pregnancies; he calls this group the "water-retention toxemias." Such toxemia may be caused primarily by low plasma proteins, excessive sodium intake or, in many cases, both. Anemia, primary renal failure and a rise in intercapillary pressure, as with congestive heart failure or venous obstruction, are conducive to water retention.

Smith and Smith⁸ show that the urinary excretion of estrogenic compounds from the fifth month of pregnancy to term in pre-eclampsia and eclampsia is considerably less than it is in normal pregnancy. In their cases, the level of serum estrogenic substance also failed to show the rise characteristic of normal pregnant women. Venning⁹ and Weil¹⁰ state that the excretion of pregnanediol in normal pregnancy gradually increases until term, but in toxemia there is a sharp decrease. Smith, Smith and Pincus¹¹ show that the ratio of estriol to estrone is about 15:1 in the last month of normal pregnancy, but in pre-eclampsia and eclampsia, this ratio is considerably lower. Pincus and Zahl¹² indicate that the corpus-luteum hormone, progesterone, facilitates the conversion of estrone into estriol, and that the excretion of sodium pregnanediol glucuronide reflects the action of progesterone. The urinary chorionic gonadotropic hormone in normal pregnancy has a peak of excretion in the early months (the twentieth to the fiftieth day after the missed menstrual period, according to Evans et al.,¹³ and at about two months according to Smith and Smith⁸); after this peak is reached, the excretion decreases rapidly and remains constant until term.

Smith and Smith^{14, 15} have shown that the placentas from pre-eclamptic and eclamptic patients contain an abnormally high concentration of prolactin, and that the estrogenic content of these placentas is low; furthermore, the serum prolactin is usually high in pre-eclampsia and eclampsia. They found that low or decreasing pregnanediol and estriol, a high or increasing percentage of estrogenic activity accountable to estradiol, decreasing or absent estrone, and high or increasing ratios of estrogenic potency after hydrogenation characterized the urines of every toxemic case. They believe that toxemia of pregnancy is closely associated with a progressive deficiency of progesterin, a concomitant decrease of estrogen and a

*Instructor in obstetrics, Boston University School of Medicine, second assistant obstetrician, Massachusetts Memorial Hospital.

consequent changed metabolism of estrogen involving greater and more rapid destruction.

Weiss et al.,¹⁶ in a study of a series of autopsies on women who died of eclampsia, noted rapid improvement after the uterus was emptied. In 16 cases in the series, death of the fetus in utero did not result in improvement of the patient. After fetal death, hormones originating in the placenta continued to be eliminated in the urine. The authors believe, since there is no valid evidence that pressure on the ureter or renal artery, primary kidney disease, infection or nutritional disease is primarily responsible for the syndrome, that the presence of a functioning placenta maintains the syndrome and that removal of the placenta is responsible for the improvement. No identifiable chemical substance was found to be responsible. Extracts of placentas from normal or toxemic pregnant women failed to yield pressor substances. Weiss and his associates do not believe that the syndrome occurs spontaneously or has been induced in animals. Their experiments in nonpregnant and pregnant rabbits and rats with Pitressin, estrogenic substances, progesterone, pregnancy-urine prolan, desoxycorticosterone and placental extracts failed to produce the syndrome. They consider the changes observed in the kidneys and other organs during the course of the syndrome secondary to the suspected chemical or "hormonal" changes, but in severe cases this secondary damage to the kidneys and liver can play a role in the vicious circle leading ultimately to convulsions, acidosis and circulatory collapse. They believe that the primary factor initiating the syndrome originates from the placenta; it may be a normal hormonal constituent of pregnancy in abnormal amounts, or in normal amounts acting on a vascular system with a congenital or acquired hyperirritability.

It seems, from the theories discussed, that whatever its cause, eclampsia affects first, or even arises from, the placenta. The chief pathologic damage is to the vascular system. And, possibly, it may have a hormonal origin.

PHYSIOLOGIC PATHOLOGY

A major abnormality during pregnancy is sudden increase in weight due to edema. Water retention can be caused by changes in sodium balance brought about by a high salt intake, or by a large amount of sodium bicarbonate taken for "heart burn."⁷ Anemia, for an unknown reason, is also conducive to water retention. Hormone balance plays a part in water retention, and vitamin lack, diabetes and anything else that disturbs the blood supply to the placenta may cause hormonal

imbalance. Decrease in plasma protein is another important factor in water retention; the albumin fraction is four times as active osmotically as the globulin fraction, so that it is essential to do separate analyses. Hydremia, rise in intracapillary pressure, hypothyroidism, primary renal failure and cardiac failure are other factors. Weiss et al.¹⁶ find that 64 per cent of all normal pregnant women have generalized edema of varying degree. They believe that the above factors are not the primary causes of edema, although they may play a secondary role. They suspect that, by exclusion, a chemical or hormonal etiology, resulting in retention of water and electrolytes in the tissues, is the cause. Dieckmann¹⁷ states that about 75 per cent of eclamptic women have edema. In his cases, edema was not due to hypoproteinemia. The osmotic pressure was above edema level, and the serum albumin and globulin were normal in composition. He believes the edema is due to changes in permeability of the capillary and cell walls.

Hypertension, another serious abnormality, can be caused by vascular spasm as well as by water retention. Hypertension occurring before pregnancy is usually due to one of the nephritides.

Headache and visual disturbances are believed to be the results of cerebral edema, which follows edema as considered above, and of ischemia of the brain.

PATHOLOGY

Irving¹⁸ gives a thorough review and presents additional descriptions of the pathological findings in eclampsia; he renews the belief that arteriolar derangement affecting all the terminal arterioles is the primary factor in the disease. The organs most affected are the kidneys. He gives Fahr's description of an increase in the size of the glomeruli due to swelling of the capillary walls, and a relative absence of blood cells in the capillary lumens, producing marked local ischemia. Hyaline thrombi are found within the loops. The tubules exhibit albuminous degeneration, which may advance to hyaline formation and fatty changes. Irving states that all glomeruli are not always equally involved; in some cases, individual ones may escape entirely, and the tubules draining these glomeruli are also unaffected. He believes that spasm of the afferent arterioles is the cause of this damage. Bell¹⁹ first demonstrated a massive thickening of the capillary basement membrane. Weiss et al.,¹⁶ describing kidney changes, discovered that the lesions were primarily degenerative and believed that the term "glomerulonephrosis," which has been applied to this condition, seems to be most suitable. They found hyalinization of the

arterioles in some cases. There were no specific changes in the interlobular and arciform arteries.

The liver lesions of hemorrhage, necrosis and fatty degeneration—usually predominant in the periphery of the lobule but also found in the central and midzonal portions—are reviewed by Irving,¹⁸ who places the liver damage on a vascular basis, since thromboses of the radicles of the portal vein or of the small branches of the hepatic artery in the portal space may be observed. Weiss et al.¹⁶ in autopsies on 25 women who died of eclampsia, noted liver lesions in less than half the cases. The lesions varied from mild to severe necrosis and hemorrhage in the peripheral lobules.

Irving¹⁸ describes hemorrhages in the cortex of the adrenal glands and in the capsule and parenchyma of the spleen. In some cases, necrosis in the lymphoid follicles was noted in the spleen; in others, acute inflammation in the spleen was found. Thickening of the arterioles has been observed.

Evidence of arteriolar spasm in the general peripheral circulation, as seen in the capillary loops at the bases of the nails and in the retinal vessels, is also discussed by Irving, and he states that the brain shows ischemic cellular disease, as well as vascular spasm causing necrosis and rupture of the vessel walls.

According to Hertig,²⁰ 50 per cent of uteri show bilateral cornual and subserosal hemorrhages due to arteriolar spasm. He describes the rare "eclampsia of the uterus," that is, toxic separation. He has found capillary thrombosis, petechial hemorrhage and edema at one time or another in all the organs; 60 per cent of eclamptic placentas are infarcted.

Tenney and Parker²¹ describe placental lesions consisting of a premature aging of the placenta. Although 10 to 50 per cent of a normal placenta shows syncytial degeneration, the amount of degeneration in eclampsia is over 50 per cent. This degeneration consists of a clumping together and autolysis of nuclei in the syncytial cytoplasm, clumps of darkly staining masses with no cell outline, and areas of syncytial cells without nuclei. The final stage is the disappearance of all nuclei from the syncytial layer; the villus is surrounded by a thin, irregular mass of hyaline material. Moreover, there is marked congestion of the blood vessels of the villi in the toxemic cases. The blood pressure and the albuminuria closely correlated with the placental findings in 90 per cent of the cases.

STATISTICS

At the Massachusetts Memorial Hospitals, from January 1, 1923, to November 1, 1941, there were

55 cases of eclampsia—emergency, clinic and private—among 22,089 hospital and district deliveries, an incidence of 0.249 per cent, or 1:402. There were 12 maternal deaths, a mortality of 22 per cent (Table 1). Among the fatal cases, there

TABLE 1. Mortality in Cases of Eclampsia.

SOURCE	NO. OF CASES	INCIDENCE %	MATERNAL MORTALITY %	INFANT MORTALITY %
Massachusetts Memorial Hospitals	55	0.249	22	36
Weintraub ²²	63	0.2	14	33
Ware and Noble ²³	105	2.02	15	24
Ted and Reed ²⁴	173	0.312	27	51
Torppe and Coppedge ²⁵	350		13	31
Peckham ²⁶	127		11	40
Chesley and Somers ²⁷	169	0.395	7	161
Rucker ²⁸	204		13	13
Lazar ²⁹	225		16	35
Davis and Hatzig ³⁰	879	0.576	15	24
Schwarz and Dorsett ³¹	186		7	24
Kimbrough and Shirey ³²	43	0.34	14	28
Bryant and Flemming ³³	120		2	2
Greenhill ³⁴	78	0.28	8	28
Williams ³⁵	395	0.98	17	

*Excluding babies born to mothers in postpartum eclampsia.
†Last 108 cases mortality 5.6 per cent.
‡Last 149 cases

were 2 vaginal sections, 1 classical cesarean section, 1 manual dilatation and 1 high-forceps delivery of a large baby through a generally contracted pelvis—this last patient, an emergency case, entered the hospital fully dilated and had several convulsions before and after delivery. Four patients died undelivered, 1 died of general peritonitis after a spontaneous delivery following artificial rupture of membranes to induce labor, and 2 died after normal deliveries following conservative treatment. From 1923 through 1931, when operative deliveries were prevalent, there were 32 cases of eclampsia and 9 deaths, a mortality of 28 per cent. Since then, the treatment has been conservative, and there have been 23 cases of eclampsia and 3 deaths, a mortality of 13 per cent. Twenty-nine of the patients were under thirty years of age, and 8 of these died, the mortality being 28 per cent; 26 were thirty years old or older, and 5 died—a mortality of 19 per cent.

Prenatal care is a valuable means of reducing the incidence of and the maternal deaths from eclampsia. It is considered adequate in the clinic when a patient is seen in the fifth month of pregnancy and keeps appointments at least once every four weeks until the seventh month of pregnancy, once every two weeks until the last month, and then once weekly until delivery. It is evident from the results in various clinics that the majority of cases of eclampsia occur in the group of pregnant

women who have had no or inadequate prenatal care (Table 2).

Our statistics agree with most others in that eclampsia is predominant among primigravidas (Table 3).

There was a slight seasonal variation in the incidence of eclampsia in this series, 60 per cent of

TABLE 2. Prenatal Care among Patients with Eclampsia.

SOURCE	ADEQUATE CARE	INADEQUATE CARE	NO CARE
	%	%	%
Massachusetts Memorial Hospitals	18	53	29
Kimbrough and Shirey ²²	40	27	23
Greenhill ²⁴	18	23	59
Ware and Noblin ²³	0	33	67

the cases occurring from October through March (Table 4). Kimbrough and Shirey²² in a study of 43 cases, found the incidence to be as follows: "spring," 21 per cent; "summer," 21 per cent; "autumn," 35 per cent; and "winter" 23 per cent.

TABLE 3. Comparison of Parity in Cases of Eclampsia.

SOURCE	TOTAL NO. OF CASES	PRIMI- GRAVIDAS	MULTIP- ARAS
		%	%
Massachusetts Memorial Hospitals.	55	69	31
Kimbrough and Shirey ²²	43	72	28
Greenhill ²⁴	78	73	27
Weintraub ²²	63	57	43
Teel and Reid ²⁴	173	49	51
Ware and Noblin ²³	105	86	14
Total	517		
Averages		65	35

In a report of 879 cases, Davis and Harrar³⁰ observed that eclampsia increased through January to a high point in April, with a decrease to a low point in July.

There were two sets of twins from the 50 mothers who delivered, or 4 per cent.

TABLE 4. Seasonal Incidence of Eclampsia.

SOURCE	TOTAL NO. OF CASES	NO. OF CASES A MONTH											
		JAN.	FEB.	MAR.	APR.	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.
Massachusetts Memorial Hospitals	55	7	4 (25%)	3	3	2 (20%)	6	5	2 (20%)	4	9	2 (35%)	8
Ware and Noblin ²³	105	12	8 (28%)	9	6	14 (30%)	12	14	7 (28%)	8	4	6 (14%)	5
Teel and Reid ²⁴	173		(22%)			(28%)			(27%)			(23%)	

There was 1 case of polyhydramnios in the 55 cases of eclampsia.

Fifty-two babies were delivered from 50 mothers, and 4 mothers died undelivered. There were 13 stillbirths, and 3 babies died after birth, making an uncorrected total of 20 deaths, a mortality rate of 36 per cent. One woman, after subsidence of convulsions and symptoms, went home undelivered, against advice.

The fetal ages when eclampsia occurred are shown in Table 5. Ware and Noblin²³ report in-

TABLE 5. Fetal Ages When Eclampsia Occurred.

SOURCE		MONTHS						
		5 %	6 %	7 %	7½ %	8 %	8½ %	9 %
Massachusetts Memorial Hospitals		2	4	13	9	27	7	38
Weintraub ²²		0	5	16		16		63

cidences as follows: five months and under, 6 per cent; premature, 57 per cent; and full term, 37 per cent.

The times that convulsions occurred are given in Table 6.

SIGNS AND SYMPTOMS

The most frequent signs and symptoms before convulsions in this series were albuminuria (96 per cent), hypertension (93 per cent), edema (82 per cent), headache (71 per cent), blurring of the eyes or spots before the eyes (38 per cent), vomiting (35 per cent) and pain (25 per cent).

The blood uric acid was recorded in 48 cases. The highest readings before, during or after convulsions in 38 patients who recovered averaged 5.8 mg. per 100 cc., and for 10 of the women who died the average was 7.1 mg. per 100 cc., in comparison with Stander's³⁶ figures of 5.6 and 7.6 mg. per 100 cc., respectively. Six of the recordings had readings of 3.5 mg. or below. According to Chesley,³⁷ the absolute level of uric acid is often elevated. More generally, the ratio of uric acid to nonprotein nitrogen is increased, the upper normal ratio being about 1:10. The cause of a rise in uric acid in eclampsia is not known. However, Cadden and Stander,³⁸ in a study of 5 cases,

showed that eclampsia is not associated with decreased excretion of uric acid, and they believe that an elevated uric acid is probably due to impaired destruction of uric acid in the liver.

Routine determinations of the carbon dioxide combining power were not done. Stander and Radelet,³⁹ as well as Cadden and Stander,³⁸ find a decrease in the carbon dioxide combining power. Cadden and Stander emphasize the value of

determining the carbon dioxide combining power and the uric acid. They believe that such data are more indicative of an impending development of convulsions than hypertension, amount of albuminuria or other symptoms are.

TREATMENT

The usual nursing routine in conservative treatment is followed. The patient is placed in a quiet, darkened room. A nurse is always in attendance and she is warned to stop the patient from choking,—because of saliva, vomitus or swallowing the tongue,—to prevent biting of the tongue, and to

When the above treatment fails to improve the patient, a venesection is sometimes done to lower the systolic blood pressure 30 to 50 mm., 200 to 400 cc. of blood being withdrawn.

Besides the routine treatment for pulmonary edema in eclampsia, Dean⁴⁵ recommends bronchoscopy.

As soon as convulsions are controlled and the patient appears improved, and at times when the patient does not improve and it is considered desirable to avoid further delay, the membranes are ruptured. If the cervix is not sufficiently softened, it is packed for twenty-four hours. If the patient

TABLE 6. *Times When Eclamptic Convulsions Occurred.*

SOURCE	ANTE PARTUM	INTRA PARTUM	POST PARTUM	ANTE AND INTRA PARTUM	ANTE AND POST PARTUM	INTRA AND POST PARTUM	ANTE, INTRA AND POST PARTUM
	%	%	%	%	%	%	%
Massachusetts Memorial Hospitals	42	13	18	9	5	7	5
Weintraub ²² . . .	64	19	18				
Ware and Noblin ²³	82	2	13	1			2
Williams ³⁰ . . .	53	25	22				

record the blood-pressure and pulse rates hourly. The foot of the patient's bed is elevated, if necessary. A Foley catheter is inserted, and the catheterized urine examined. Blood is taken for determinations of uric acid, carbon dioxide combining power, nonprotein nitrogen, sugar, protein and albumin-globulin ratio. Oxygen is given for cyanosis. Sodium phenobarbital, 5 gr., is given intramuscularly, and Sodium Amytal, 3 gr., is given by mouth or rectum to prevent restlessness (morphine sulfate is occasionally given). Fifty cubic centimeters of a 50 per cent glucose solution intravenously is given slowly to withdraw fluids from the edematous tissues, to increase urinary output and to combat acidosis.^{40, 41} However, dehydration is not a strict rule. If there is oliguria, 500 to 1000 cc. of 10 per cent glucose in distilled water is given intravenously. This is repeated if necessary for the treatment of oliguria or concentration of the blood, according to Davis⁴² and Dieckmann.⁴³ Davis says that when more than 200 gm. of glucose is given rapidly, it causes a very marked glycosuria. Twenty cubic centimeters of a 10 per cent magnesium sulfate solution is given intravenously at each convulsion, and between convulsions if the blood pressure starts rising. Not more than 10 gm. of magnesium sulfate has been given in twenty-four hours. Fischer⁴⁴ reports that it is safe to give up to a total of 8 gm. in twenty-four hours, as a 2.0 or 2.5 per cent solution. Torpin and Coppedge²⁵ give up to 24 gm. in twenty-four hours and 3500 cc. of a 5 per cent glucose solution, with good results. Fluids must be restricted in cardiac cases.

is a primipara with a long, hard cervix and a prolonged labor is feared, or if there is a cephalopelvic disproportion or any other contraindication to pelvic delivery, such as lower-segment fibroids or an amputated cervix, the patient is put in as good condition as possible, blood donors are kept available, and a cesarean section is performed.

Ware and Noblin²³ give digitalis routinely when using magnesium sulfate, because they believe that it should tend to overcome a cardiac depression produced by intravenous magnesium sulfate, since digitalis and magnesium sulfate are physiologically antagonistic in their action on the heart.

Smith and Smith⁴⁶ have used progesterone and estrogen in the treatment of toxemia, but they consider these drugs of little benefit when eclampsia has developed. They advise frequent prolan determinations and early hormonal treatment in pre-eclampsia. They realize that the expense of prolan determinations and hormonal treatment precludes this method at present.

Bryant and Flemming²³ report the use of veratrum viride in the treatment of eclampsia. This drug has been tried by many physicians in the past years. It was used at the Massachusetts Memorial Hospitals in 1912-1913 in doses up to 230 drops by mouth in eleven and a half hours and 360 drops subcutaneously in seventy-two hours, and it did appear to cause a drop in pulse rate; the blood-pressure recordings were inadequate. It was discontinued because it did not seem to give improved results. However, in those years, oh

stetric treatment was radical, including *accouchement forcé*, and little or no treatment for shock; moreover, without intravenous magnesium sulfate therapy, it is difficult to see how any medical treatment could have had a fair trial. Workers at the Cincinnati Hospital, using veratrum viride, intravenous magnesium sulfate, concentrated glucose solutions, sedatives only for extreme restlessness and labor and, rarely, morphine, have treated 120 consecutive cases of eclampsia with 2 deaths, a mortality of less than 2 per cent, which is remarkable.

Veratrum viride is regarded as a powerful drug, and individual susceptibility to the drug is marked. It is described as being a vasodilator, and spasm of the blood vessels is therefore relieved and the blood supply to the tissues is increased.

It seems apparent that veratrum viride should be used with great caution. Until results are obtained from others who are now using the drug according to the routine of Bryant and Flemming,³³ it should not be routinely employed. If the mortality rate of eclampsia can be lowered in other hospitals, it is evident that veratrum viride has an important place in treatment.

SUMMARY AND CONCLUSIONS

Recent theories on the cause and results of eclampsia are reviewed. The physiologic and cellular pathology is discussed, the damage caused to the vascular system being stressed.

Statistics of 55 consecutive cases of eclampsia, with comparative statistics, are presented.

The treatment of eclampsia is outlined. Since the mortality rates show that treatment continues to be inadequate, conservative therapy should be employed until a better method can be substantiated.

99 Bay State Road

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DIABETES INSIPIDUS AND PREGNANCY¹

Report of Two Cases

HARRY BLOTNER, M D,[†] AND PAUL KUNKEL, M D[‡]

BOSTON

DIABETES insipidus is comparatively rare, and the combination of this disease and pregnancy is still rarer. It is seldom met with in practical obstetrics, and since 1915 there have been only 3 such cases in approximately 50,000 deliveries at the Boston Lying-in Hospital. From the scarcity of reported cases of the combination of pregnancy and diabetes insipidus, the impression is obtained that very few patients with this disease have children. However, in a thorough study of the literature, it was found that patients with diabetes insipidus have children more frequently than one would expect.¹ At times they are quite prolific, some having as many as eleven children during the course of the disease.

One of the most interesting cases to illustrate this point was reported by Bellot and Brougnart² to the Philomathical Society on October 22, 1791. The patient was a forty-year-old Frenchwoman, who was married at the age of twenty-two. She had had a very considerable thirst from her earliest infancy. While she was single, she drank three pailfuls of water a day. After she was married, two pailfuls were sufficient until she was delivered of her first child, when she returned to her former quantity of three pailfuls and continued it until after the birth of her fourth child. After that period, she drank only two pailfuls in twenty-four hours. When she was pregnant, she had much more thirst than usual. She had eleven children in ten pregnancies. In the presence of a commission, this woman drank 14 liters of water during the space of ten hours. One of Gee's³ patients had nine children. Weil⁴ and his son⁵ studied five generations of a family of 220 members, headed by a man with diabetes insipidus, of whom 35 had the disease. Some of the women with diabetes insipidus had eight or nine children, with normal pregnancies and birth, except that the pregnancies usually increased the symptoms of the disease.

On the basis of a perusal of the literature, the clinical effects of the combination of diabetes insipidus and pregnancy may be classified as follows: aggravation of the disease during pregnancy; transient diabetes insipidus during pregnancy; amelioration of the disease during pregnancy; no effect

of pregnancy on the disease; onset of the disease during pregnancy and persistence after delivery; and transient appearance of the disease after delivery.

Aggravation of Diabetes Insipidus during Pregnancy

A number of reports indicate that the polyuria and polydipsia of diabetes insipidus may be increased by varying degrees and during various periods of pregnancy,⁶⁻¹⁰ as already mentioned. Among 26 members with diabetes insipidus in a family of 73, Ellerman¹⁰ found increased diuresis during pregnancy of the women with diabetes insipidus. In 1 patient, who gave birth eight times, the diuresis increased during each pregnancy from around 10 to approximately 20 liters daily; during the seventh pregnancy, the daily quantity of urine reached 30 liters.

Transient Diabetes Insipidus during Pregnancy

The greatest number of reports on any one of these phases of diabetes insipidus and pregnancy appear in connection with the transient occurrence of the disease during a normal pregnancy.¹¹⁻²⁰ The disease may occur in an apparently normal woman during any stage of pregnancy, from the beginning to near the end of term. However, in most cases, the diabetes insipidus was apparent in the latter half of pregnancy, usually in the fifth or sixth month. Ordinarily, the polyuria and the polydipsia abruptly ceased two or three days after delivery, although in some cases it persisted for as long as seventeen days post partum. There have been cases in which the transient diabetes insipidus occurred in successive pregnancies, in approximately the same months of gestation. In most of these cases, the fluid intake and output increased to about 10 or 12 liters. However, in Edelmann and Kritzman's²² case, the daily urine volume reached a level of 25 liters. Novak's¹⁷ case was of interest because the diabetes insipidus appeared in the course of the first pregnancy and disappeared after delivery; this phenomenon reappeared in the course of ten pregnancies. Gansslen and Fritz¹⁰ presented an unusually interesting case of a healthy woman whose husband had diabetes insipidus. During the terminal part of her first pregnancy, she showed symptoms, which disappeared after delivery. The baby of this pregnancy subsequently had diabetes insipidus. During her second preg-

¹From the Medical Clinic, Peter Bent Brigham Hospital and the Boston Lying-in Hospital.

[†]Associate in Medicine, Peter Bent Brigham Hospital.

[‡]Formerly research fellow in obstetrics, Boston Lying-in Hospital.

nancy, which resulted in a healthy baby, the patient had no polyuria. The authors suggested the possibility that the hormone of the sick child was transferred to the mother during the terminal part of pregnancy and gave her the symptoms of the disease.

Amelioration of Diabetes Insipidus during Pregnancy

Several reports have shown that pregnancy occurring during the course of diabetes insipidus resulted in an amelioration of the disease, and after delivery the polyuria and the polydipsia reappeared abruptly.^{9, 12, 16, 30-34} The most interesting report on this aspect of the problem is that given by Duvoir, Pollet and Cachin,³³ who treated a woman with diabetes insipidus during the course of three pregnancies and observed that the polyuria decreased in the sixth month of each and that the amount of urine became normal during the weeks preceding delivery. However, on the day following delivery, the daily urine increased suddenly to 12 liters, the level before pregnancy. Carter³⁴ noted that a patient had less thirst in the seventh month of pregnancy, and that after a premature delivery, the diabetes insipidus was considerably relieved and remained so during the years of subsequent observation.

No Effect of Pregnancy on Diabetes Insipidus

A number of studies show that pregnancy had no effect on the polyuria and the polydipsia of diabetes insipidus.^{31, 35-40, 65} Some of these patients had urine volumes as high as 16 to 20 liters a day. The patients of Boissard³⁵ and Artaud³⁸ excreted similar amounts of urine without any alteration during pregnancy.

Onset of Diabetes Insipidus during Pregnancy

French³¹ observed a woman who developed diabetes insipidus with a daily urine volume of 10 liters during the fourth month of her fifth pregnancy. The polyuria and polydipsia persisted after delivery. Vickers⁴¹ treated a patient who developed diabetes insipidus with an output of approximately 8 liters when she was three months pregnant. She had urinary retention and, as a result, had to be catheterized; 3250 cc. of urine was obtained. She miscarried a normal three-month-old fetus, and the diabetes insipidus persisted after the miscarriage.

Transient Diabetes Insipidus after Delivery

Transient diabetes insipidus may also appear shortly after delivery. Laurentie and Basiliou⁴² presented the case of a thirty-seven-year-old woman who went through a normal pregnancy. On the day after delivery, the patient suddenly began

to void frequently and to drink with a "rage." Twenty-one days later, she developed violent frontal headaches, photophobia and convulsions. In addition, a transient hypertension appeared. The whole picture was typical of eclampsia; however, there was no albumin in the urine. The fluid intake was as high as 15 liters a day. At one time, the patient had to be catheterized because of a dilated bladder, and 3 liters of urine was obtained. Within six weeks after the onset of convulsions, all symptoms disappeared, and the patient was discharged from the hospital completely recovered.

There are a number of miscellaneous reports on pregnancy and diabetes insipidus, although many of them do not add individual case reports.⁴³⁻⁵³ It appears, however, that the various authors have had experience on this subject. Theses have been published by Jansen⁴⁶ and Schellenberg.⁴⁷ Jansen added a case of a woman who had six deliveries, but the diabetes insipidus appeared only during the last three pregnancies and lasted, each time, until fourteen days post partum. Discussions on this problem have been presented by Lauter and Hiller,¹⁸ Skrobanski,⁴⁹ Kleinwächter⁵⁰ and Henriet.⁵¹

CASE REPORTS

CASE 1. A 28-year-old woman, who had had diabetes insipidus for over 9 years, had been observed by one of us (H. B.) for 8 years, during which various data were obtained. The daily fluid intake and urine volume usually varied from 10 to 12 liters. The past and family histories were irrelevant. The menses were normal, except that the intramuscular injection of pituitary extract caused painful menses. General physical examinations were normal, except that the patient was about 15 pounds under weight.

The basal metabolic rate was -18 per cent. Lumbar puncture showed a normal spinal fluid. The blood Wassermann reaction was negative. X-ray examination of the skull was negative. The patient required 1 cc. of pituitary extract intramuscularly three or four times a day to reduce her fluid intake and output to about 3 liters. In the preceding 2 years, she had taken powdered pituitary extract intranasally five or six times a day, with relief. Blood studies made before pregnancy were essentially negative, both with and without pituitary extract; some of the results are shown in Table 1.

In 1936, because of various reports suggesting that the administration of estrogenic substance may suppress the diuretic principle of the anterior pituitary gland,⁵⁴ the patient was injected with 20,000 units of amniotin daily for 10 days, without any effect on the fluid intake and output.

The patient had her last menstrual period on June 24, 1940. Her expected delivery date was March 31, 1941. Physical examination was negative except that she weighed only 100 pounds, which was low for her height of 65 inches. The pregnancy progressed normally for both patient and fetus. She had no nausea or vomiting at any time and felt just as well as when she was not pregnant. During the beginning of pregnancy, the daily fluid intake and output were about 10 to 12 liters, the level before

conception, and she took powdered pituitary extract intranasally, with a reduction in these volumes. She felt movements of the fetus in the 5th month. The blood pressure remained constant at approximately 120/70. X-ray films of the pelvis taken on December 31, at the end of the 6th month of pregnancy, showed a fetus consistent with the date.

The daily fluid intake and output are of unusual interest because they increased to a level of about 13 to 15 liters at the end of the 7th month of pregnancy. When the patient was 7½ months pregnant, the polyuria and polydipsia began to decrease appreciably so that shortly before delivery the daily fluid intake and output were about 3 liters for some days (Fig 1). She went through

was normal. The placenta appeared normally mature.

At birth, the baby's weight was 8½ pounds, and its height 55 cm. There was an initial loss of 12 ounces, but the birth weight was regained on the 10th day. The baby was breast fed for 31 days. There was inadequate milk supply during this time, but subsequently the mother's breasts dried up rapidly and the baby was given a milk formula. At the age of 6 months, the baby weighed 16 pounds and had one tooth. At 8 months, his weight was 20½ pounds and his height 74 cm. He had been perfectly normal and had taken a normal amount of liquids.

Various laboratory data were obtained on this patient before during and after pregnancy (Table 1). The re-

TABLE 1 Laboratory Data before during and after Pregnancy

Date	Weight lb	BLOOD VOLUME			Hematocrit		Serum Protein	Cholesterol	Basal Metabolic Rate	Pituitary Extract Given	Fluid Intake liter
		Total Vol. cc	Plasma Volume cc	Corpuscul. Volume cc	%	%					
Before pregnancy											
With therapy	100	—	—	—	35	65	7.0	144	1	No	11.0
Without therapy						65	6.4	154		Yes	3.0
During pregnancy											
1/20/41	111	460	310	14	31	69	6.4		5	No	13.0
2/1/41	113	4950	3460	149	30	0	6.3		11	Yes	5.5
3/1/41	113	4810	3360	145	0	0	6.1	275	5	No	4.1
3/9/41	115	4990	3450	145	28	72	6.1	215	-1	Yes	7.7
After delivery											
4/9/41	101	3450	2300	115	4	96			19	No	5
4/10/41	101	341	2500	116	4	96			0	Yes	7.8

a normal labor and was delivered of a normal baby on March 28. The convalescence was normal. The day after delivery, the fluid intake and output increased abruptly to a level of 8 liters, and remained at approximately that level during the subsequent 9 months of observation. These volumes were somewhat lower than those noted before pregnancy. The patient had no edema at any time during or after pregnancy.

It was interesting that during pregnancy the administration of pituitary extract caused a sensation of constriction of the uterus and that as a result, the extract was administered only in small doses. However, when Pitressin, which is supposedly pituitary extract without the oxytocic principle, was administered, it had an antidiuretic effect, without the constrictive action on the uterus. This was shown experimentally by the use of a tocograph which, when properly placed on the abdomen, mechanically records and times the uterine contractions. No uterine contractions were elicited when 0.5 cc of Pitressin was injected subcutaneously. However, normal and rhythmic uterine contractions were obtained when 0.5 cc of pituitary extract was injected.

The placenta weighed 840 gm and measured 23 by 20 by 2.5 cm. The membranes were complete. The cord was attached 2 cm from the nearest placental margin, measured 45 by 1 cm, and was normal on section. The fetal surface was shiny, bluish gray. The maternal surface was intact and very fissured, deep red dish gray and soft. The cut surface was deeply congested and soft. Microscopically, there was a moth-eaten and fibrinoid degeneration of the decidua. There were foci of recent hemorrhage on the decidua. The villi were slightly larger than normal ones at full term but were well vascularized. The syncytial nuclear knots were in frequent. The stroma was not remarkable. The chorion

sults of the blood volumes were approximately the same as those found during and after pregnancy in the normal woman. In the terminal part of pregnancy, the hematocrit showed a decreased percentage of corpuscles, which increased to 34 per cent shortly after delivery. This compared with 35 per cent obtained a number of times before pregnancy. The venous pressure was equivalent to 10 cm of water. The circulation time was 14 seconds.

TABLE 2 Sugar Tolerance Tests before during and after Pregnancy

Date	BLOOD SUGAR LEVELS					PITUITARY EXTRACT GIVEN
	FASTING mg / 100 cc	1/2 HR mg / 100 cc	1 HR mg / 100 cc	2 HR mg / 100 cc	3 HR mg / 100 cc	
Before pregnancy						
4/1/33	66	314	—	159	54	No
4/11/33	61	196	214	133	57	No
During pregnancy						
3/8/41	100	16	1.2	135	116	No
3/11/41	92	14	16	127	127	Yes
After delivery						
4/7/41	105	145	1.8	135	116	No
4/9/41	131	145	16	133	145	Yes

by the cyanide method. The basal metabolic rate increased toward the end of the pregnancy to +1 per cent, but within 10 days after delivery, it had decreased to -19 per cent, the level before pregnancy.

Sugar tolerance tests were made during and shortly after pregnancy, and these results were much the same. However, the blood sugar curves were lower than those obtained several years before pregnancy, as shown in Table 2.

CASE 2. A 36-year-old woman was seen in consultation by one of us (H. B.) with Dr. Henry S. Finkel, who treated her during her pregnancies. The family, past and menstrual histories were irrelevant. In 1936, she was delivered of a female child by low cervical cesarean section after a long test of labor, because of cephalopelvic disproportion. There was no polyuria or polydipsia at that time or immediately thereafter.

In the present pregnancy, the last menstrual period began on August 17, 1941. The expected date of confinement was May 24, 1942. General physical examination and routine blood and urine tests were negative. The height was 64 inches, and the weight was 140 pounds. The pregnancy progressed normally until about the 5th

DISCUSSION

A review of the literature indicates that pregnancy may aggravate, ameliorate or not influence diabetes insipidus. In addition, the disease may appear during any stage of pregnancy, disappearing or persisting after delivery. In the first case presented, the polyuria and polydipsia showed some increase in the seventh month of pregnancy and a gradual reduction during the eighth month, so that for some days before delivery the fluid intake and output were about 3 liters. After a

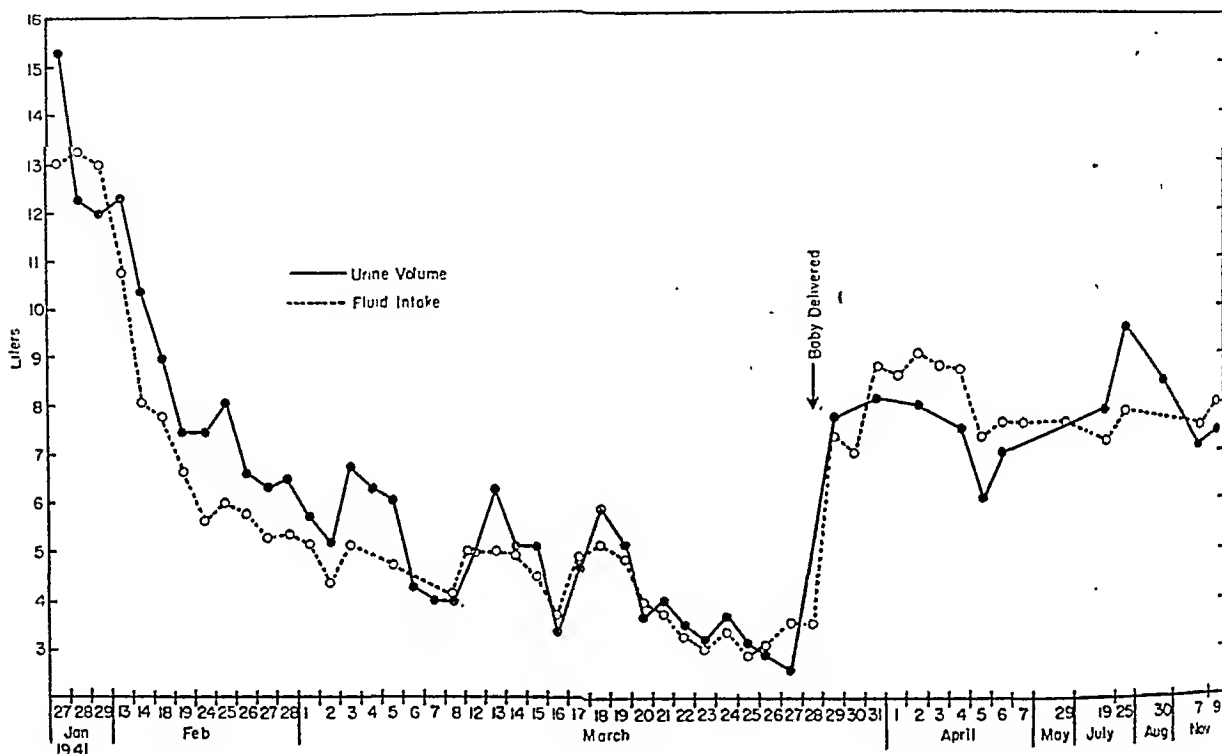


FIGURE 1.

This chart records the daily fluid intake and urinary output during the last two months of pregnancy and after delivery of the patient in Case 1; during this period, no pituitary extract was administered.

month, when the patient began to notice polydipsia and polyuria, which increased progressively as the pregnancy advanced. There was no unusual weight gain. During the last 2 months of pregnancy, the average daily fluid intake and output were about 8000 cc., with maximum and minimum levels of 9200 and 7600 cc. The urine had a specific gravity of 1.002.

On April 27, 1942, x-ray examination revealed a twin pregnancy. Because of the excessive size of the abdomen and the extreme discomfort of the patient, she was delivered prematurely on May 6, 18 days before term, by a low cervical cesarean section under spinal anesthesia. Normal twin boys weighing 5¾ pounds and 7½ pounds, respectively, were delivered. There was a double-ovum, twin, fused placenta.

The convalescence was uneventful except for considerable abdominal distention for the first few days. The polydipsia and polyuria disappeared abruptly after the delivery. The fluid intake and output were normal during the subsequent 3 months of observation. The specific gravity of the urine increased to about 1.015.

normal delivery of a normal baby, the polyuria and polydipsia suddenly rose to about 8 liters, which was somewhat lower than the level before conception took place. In the second case, transient diabetes insipidus appeared in a normal woman in her fifth month of pregnancy and disappeared suddenly after delivery by cesarean operation.

The cause for these variable effects of pregnancy on diabetes insipidus is conjectural. The excretion of water is controlled by a balance of the hormones that diminish and those that produce diuresis. Dexter and Weiss⁵⁶ believe that the mechanisms of oliguria of pregnancy are not uniform in the absence of cardiac or renal disease. The variable effects apparently depend on which of these hormonal forces predominates. It is suggested that

the diuretic or antidiuretic hormone of the fetus may be transferred to some mothers and produce the effects of each in the mother. In the first case presented above, a marked improvement in the diabetes insipidus toward the end of pregnancy was conceivably due to the antidiuretic action of the posterior pituitary lobe of the fetus or to the increased activity of that of the mother. On the other hand, the patient of Gansslen and Fritz²⁰ suggests the possibility that the diuretic hormone of the fetus was transferred to the mother, with the resultant temporary symptoms of diabetes insipidus.

The hormones that diminish diuresis include the hormone of the posterior pituitary lobe. Its value is well established. In addition, follicular hormone, which is normally increased during pregnancy, has been used with success in the treatment of polyuria without pregnancy by Troisier⁵⁷ and Beltrametti,⁵⁸ although this effect was not observed by Blotnei.⁵⁴ The former injected large doses of folliculin into patients with diabetes insipidus and obtained a marked antidiuretic effect. In the first case presented above, no such effect was obtained before pregnancy. Müller³⁰ referred to Scanzoni, who observed a nonpregnant woman with sparse menses and polyuria and noted that when the menses became regular the polyuria diminished.

The diuretic hormones are most probably of anterior pituitary or placental origin. Henriet⁵¹ referred to Lévy-Solal, who presented a polyuric patient with a hydatidiform mole, a condition in which the urinary prolan is markedly increased. In addition, Lévy-Solal observed a pregnant woman who, in spite of edema, had a significant polyuria. The determination of her daily prolan excretion gave the enormous figure of 38,000 rabbit units.

The diuretic action of the thyroid hormone is also known. However, in the first case reported above, the thyroid gland probably had no effect on the polyuria because the metabolism increased from -18 to +1 per cent when the urinary volume had dropped to 3 liters a day. After delivery, the patient's metabolism decreased to -19 per cent, and polyuria again developed. The combination of these findings is contrary to those observed by Blotnei and Cutler⁵⁰ in patients with diabetes insipidus whose polyuria was relieved by total thyroidectomy.

The blood volumes determined with Evans blue^{60, 61} were of interest because they were normal in spite of the interchange of huge volumes of fluids. The administration of pituitary extract did not dilute the blood or change significantly the blood volumes either during or after preg-

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MEDICAL PROGRESS

MILITARY DERMATOLOGY

C GUY LANE, M.D.*

BOSTON

MILITARY dermatology concerns all cutaneous manifestations that are presented to medical officers under war conditions. Wherever medical officers may be ordered for duty over the present and future world wide battlefronts, they cannot avoid being presented with cutaneous problems. Not all these physicians will have dermatologists available for consultation, and each officer will often be compelled to decide independently on these problems in military dermatology. Many of the diseases are infections caused by animal and vegetable parasites and the pyogenic organisms. The general principles of preventive medicine apply particularly to this group of cutaneous diseases. The medical officer has as his patients healthy young adults. He has the organization and discipline at hand for their control. His duty is to lessen disability and prevent "days lost" from active duty. Detection of disease and the correct diagnosis are the first necessity. With this knowledge, steps may be taken to prevent the disease and to avert its extension on the surface of the patient, its appearance in others and its complications. In the prevention of complications, attention should be given to avoiding not only the complications of the disease but also those of therapy — a significant point in the treatment of cutaneous disease. In the field of cutaneous medicine, as well as in other diseases in wartime, prophylactic measures are essential.

That this prevention is a necessary and vital factor is indicated by a review of the report on skin diseases published by the Surgeon General's office in 1928. This report¹ begins as follows:

Diseases of the skin, exclusive of dermatological manifestations of venereal disease, though ordinarily considered to be of minor importance in so far as danger to life is concerned, are of great importance to an army operating in the field by reason of the non-effectiveness they cause. This was true of past wars and equally so of the World War.

There is no reason to expect that this statement will not be true in the present war, although a full utilization of the knowledge of

cutaneous disease, if such knowledge could be applied, would certainly lessen the duration of disability and the incidence of disease.

The report summarizes the dermatologic figures for the Civil War as follows: itch, 35,236; skin diseases, 38,946; a total of 74,182 cases. Perhaps only these two skin diseases were recognized eighty-two years ago. In the statistics for World War I, the report includes relatively few cutaneous disorders, only about 126,000 cases being listed (Table 1). However, a review of this list indicates very

TABLE 1 Diseases of the Skin and Cellular Tissue Resulting in Primary Admission to All United States Army Hospitals, April 1, 1917, to December 31, 1919¹

Disease	No. of Cases
Carbuncle	2,330
Furuncle	19,958
Abscess	16,329
Cellulitis	12,874
Trichophytosis	2,813
Ectoparasitism	3,269
Dermatitis	858
Eczema	4,035
Erythema	1,495
Herpes	3,141
Impetigo	2,735
Lichen	69
Pityriasis	579
Psoriasis	1,506
Syphilis	34,134
Other diseases of skin and cellular tissue	20,270
Total	176,375

clearly that many cases could not have been reported and that numerous skin diseases are not discussed. Fungus infections, for example, account for only 2000 cases, and trench feet, in another portion of the volume, for only 2000 cases. There were 3500 cases of ectoparasitism, and yet at the time of the Armistice, pediculosis probably involved 90 per cent of the men in the American Expeditionary Force. Little mention is made of the numerous secondary infections that probably occurred as a result of this infestation. A separate table indicates 18,000 cases in which skin disease was found concurrent with other disease for which hospital admission was made (Table 2). In addition, such diseases as erysipelas, anthrax, trench feet, mycoses, cancer of the skin, purpura and nail defects are not included in the special list of skin diseases.

The statement quoted above regarding non-effectiveness is borne out by the number of days lost during the war (Table 3). The figures include

Reprints of articles in this series are not available for distribution but the articles will be published in book form. The current volume is *Medical Progress Annual Vol III 1942* (Springfield Ill no 3 Charles C Thomas Company 1942 \$5.00).

*Clinical professor of dermatology Harvard Medical School and Department of Dermatology Massachusetts General Hospital.

only the diseases mentioned in the portion of the report entitled "Skin Diseases," omitting the cases found concurrently or those in the list of general diseases. It is obvious, therefore, that over 2,000,000 days of service were lost by reason of cutaneous affections to the Army alone during World War I.

Syphilis is also an incapacitating disease, this report³ stating that there were 67,026 admissions for syphilis and 9665 other cases in which syphilis was found when the soldiers were admitted for

TABLE 2. *Concurrent Diseases of Skin and Cellular Tissue Found in Cases Admitted for Other Diseases to All United States Army Hospitals, April 1, 1917, to December 31, 1919.*¹

DISEASE	NO OF CASES
Carbuncle	158
Furuncle	1 763
Abscess	3 681
Cellulitis	1 718
Trichophytosis	411
Ectoparasitism	761
Dermatitis	150
Eczema	663
Erythema	352
Herpes	572
Impetigo	328
Lichen	19
Pityriasis	238
Psoriasis	356
Scabies	2 926
Other diseases of skin and cellular tissue	4,911
Total	19 007

other reasons. It is of interest that the admissions for syphilis represented only 1.85 per cent of the admissions to hospitals, and yet the total number of days lost from duty was over 1,927,201, and 143 deaths were charged to syphilis.

The incidence of skin diseases in the Navy confirms the gravity of these diseases in a military organization. In a report by Sulzberger, MacClatchie and Parsons⁴ citing statistics of the Medical Corps of the United States Navy, 14.8 per cent of all admissions for disease between 1929 and 1938 included men with skin diseases and syphilis. It is probable that a number of skin cases were omitted from these figures, which do not include, of course, the ambulatory patients. One and a quarter million days in hospitals were lost on account of these diseases. Skin diseases represented the third commonest cause of admission in this period, with a rate of 22.6 per thousand men, acute catarrhal fever ranking highest and gonorrhea second. These are peacetime figures and do not consider the inevitable increase of certain parasitic infections in time of war. Of individual diseases, scabies had the highest admission rate and trichophytosis next, and trichophytosis ranked highest in number of sick days per year per thousand men.

In addition, a personal letter from a dermatologist at one of the naval stations shows that 13 per cent of the total admissions to the hospital in the first eight months of its existence were on the dermatologic service. This figure includes all the common diseases of the skin in stages that rendered the service men temporarily unfit for duty. Thirty per cent of these admissions were for fungus infections of the skin, and 20 per cent were for scabies. It is stated that preventive methods are in force at this particular station, and yet these admissions continue. It is furthermore of interest that almost all the patients admitted to the hospital had already been overtreated in their particular outfits. This comment of overtreatment has come to me from several other sources. The complication may occur because of the failure to make a proper diagnosis or to estimate the tolerance of

TABLE 3. *Days Lost from Active Duty in United States Army by Patients with Diseases of the Skin and Cellular Tissue (April 1, 1917, to December 31, 1919).*²

DISEASE	DAYS LOST
Carbuncle	43 000
Furuncle	212 800
Abscess	289 700
Cellulitis	223,200
Trichophytosis	45,300
Ectoparasitism	19,000
Dermatitis	12,600
Eczema	92 900
Erythema	20,500
Herpes	42,000
Impetigo	47,700
Lichen	2,200
Pityriasis	8,500
Psoriasis	42,700
Scabies	393,700
Other diseases of skin and cellular tissue	353,100
Total	1 848,900

an individual skin, or because of the desire to clear up the existing skin trouble quickly by strong measures.

It is not possible to discuss all the alterations in the cutaneous surface that may appear as a result of these diseases, but perhaps some service may be rendered by a review of some of the salient features of diseases with cutaneous manifestations that appear before medical officers under war conditions. For convenience, they have been divided into ten groups.

CUTANEOUS DISEASES CAUSED BY ANIMAL PARASITES

Parasitic diseases, both animal and vegetable, take the highest toll of disability from Army and Navy personnel. Other aspects of the parasitic diseases are often more serious than the infestation itself. Overtreatment, which has already been mentioned, constitutes a factor that definitely increases disability. The secondary pyogenic infections occurring as a complication of these parasitic dis-

eases at times assume serious aspects and are frequently a cause of prolonged disability. Perhaps more critical are diseases that the animal parasite may carry, so that the occurrence of such infestations is of particular interest from the standpoint of general preventive medicine.

Scabies ranks high in the list of these diseases that cause disability. When the disease is well marked, there is little difficulty in diagnosis. The increased itching at night, the characteristic locations of small papules and excoriations about the axillas, hands, wrists, genitals, waist and posterior upper thighs and the finding of burrows are sufficient evidence. The minimal infections in the early stages often offer considerable difficulty in the making of a definite diagnosis. In a case that has been overtreated, possibly with a mild secondary infection, a clear-cut diagnosis of scabies, pediculosis or a minimal urticaria is frequently difficult for an experienced dermatologist, and it is quite a problem for the average medical officer. Under military conditions, it is probably safer to treat such patients if there is sufficient suspicion of scabies; one should bear in mind, of course, the possibility that a dermatitis—a complicating and disabling factor—may result from therapy. Secondary pus infections of scabies are significant, and one should remember that the *Treponema pallidum* may enter through scabietic lesions.

Last year, several articles on scabies were written from the British standpoint. Buxton⁵ brought out the fact that the interval from the egg to the adult female can be less than eight days and that the first egg may be laid twenty-four hours after maturity. The female is thought to lay approximately two eggs a day, perhaps a total of forty to fifty eggs. There may be an interval of eight to ten days between infestation and the development of symptoms. The disease usually comes from another human being, but animal infestations have occasionally been discovered, although it is not possible to distinguish morphologically between the human and animal parasites.

Carter⁶ reviews the treatment of scabies with a sulfur lather tablet, but only two groups of children were treated. MacKenzie⁷ reviews the treatment of two groups of patients, one painted by a benzyl benzoate emulsion and the other by a sulfur ointment, indicating that the benzyl benzoate emulsion provided rapidity of cure, almost immediate relief from itching, ease and speed of application, and absence of unpleasant aftereffects.

Mellanby⁸ experimented with the transmission of scabies to volunteers. Of 63 persons living in underclothes and sleeping in blankets used by

known scabietic patients, only 2 became infected. On the other hand, a small number of experiments showed that scabies was conveyed by relatively slight personal contact. It is suggested that venereal contact provides better opportunity for the transmission of scabies than clothing.

Benzyl benzoate has had further favorable reports. Ingels⁹ used a mixture of benzyl benzoate, sapo mollis and isopropyl alcohol in 90 patients, with good results, and Goldman¹⁰ devised a cream modification that has proved effective, although it is more expensive than sulfur ointments.

In the Navy, Nolan¹¹ has used a soap paste, containing 18 per cent sulfur, that is efficient and inexpensive, but a three-day course of treatment is necessary. Rotenone has been reported to be successful in scabies, but Epstein¹² believes that it is ineffective in the presence of a complicating pyoderma.

Although these methods are successful in the treatment of scabies, they do not appear to be any more speedy and efficient than the present twenty-four-hour treatment with Danish ointment,¹³ if the preparation can be compounded correctly and made available for use by the armed forces at the places where it is needed.

In any discussion of scabies, consideration must be given to the atypical cases, which may be difficult to detect, and to the minimal infestations, which are not sufficient to bring the patient to sick call. Search should always be made for contacts and sources of infestation, to eradicate them. Sterilization of clothing (bed and body) is essential. Too much emphasis cannot be placed on early detection and, perhaps, on the periodical inspection of troops for minimal lesions if a case or cases are discovered in a particular camp.

Pediculosis, of course, should be easy to recognize. The finding of nits in the scalp or the pubic region on careful inspection quickly confirms the diagnosis. The body cases, with minimal signs, are often difficult, and yet they may remain as a source of infestation to others. The secondary infections, as a result of infestation, will undoubtedly be markedly increased in the tropical cases, and antiseptic therapy, as well as antiparasitic therapy, should be undertaken. A 2.5 per cent solution of phenol applied for one hour and followed by combing with a fine-toothed comb is a satisfactory form of treatment for the scalp variety. The pubic cases clear quickly following shaving of the entire affected area. A shower and sterilization of clothing are necessary. Delousing stations, with bathing facilities and clothing sterilization, will adequately clear the body type.

TROPICAL SKIN DISEASES

Tropical skin diseases will need consideration by American physicians more than in any other war. Many varieties of cutaneous disease are due to fungi, protozoa and metazoa. The manifestations vary with the particular section of the world to which a medical officer may be assigned, and no definite review of these diseases is possible. Strong's¹⁴ recent revision of Stitt's well-known book is worth studying for those ordered to tropical countries. The secondary pyogenic infections of these infestations will undoubtedly be a further cause of disability. Adequate precautions will need to be taken to prevent the invasion of this country by these diseases as the troops return home.

DISTURBANCES CAUSED BY VESICANT CHEMICAL-WARFARE AGENTS

Chemical-warfare agents caused considerable injury and some deaths during the last war. The principal vesicants are mustard gas and lewisite. Mustard gas, recognized clinically by the garlic-like odor and brownish oily stains on the clothing, is of low volatility, and may remain in the open for ten days—longer in the woods and in cold weather. After a latent period of two to six hours, the gas causes erythema with itching and burning, and the absorption of the liquid begins in three minutes if it contacts the skin. Vesicles and bullae are rapidly produced and heal slowly. In contrast to mustard gas, lewisite, which has a geraniumlike odor, has a shorter latent period,—fifteen to thirty minutes,—and there may be more sneezing and nasal irritation. The bullae form more quickly, and because of the arsenic content, varying degrees of arsenic poisoning are produced by the cutaneous lesions. With both, if the patient is seen early, the removal of clothing for decontamination is necessary, and the skin should be treated with solvents (kerosene, gasoline and so forth) or oxidizing agents (bleaching-powder paste, dichloramine T, hydrogen peroxide and sodium bicarbonate).

Goldman and Cullen²² have recently reviewed the effects of these agents and their treatment. The subject is also presented in a seventy-five-page booklet issued by the Office of Civilian Defense.²³ The later treatment of burns by these agents is well outlined by MacCollum.²⁴ If assigned to front-line duty, the medical officer should be familiar with the protective methods against these agents, their first-aid care, their aftercare and the details of decontamination.

SYPHILIS

Syphilis deserves further comment. Early primary and secondary syphilis will undoubtedly be seen. It should be detected early and treated ade-

quately. The cases should be sent to special centers for treatment until noncontagious, and provision should be made for uninterrupted continuous treatment²⁵ in accordance with accepted procedure. If the war lasts five years, attempts to conserve manpower by adequate early treatment are particularly necessary. At present, the new five-day treatment²⁶ or one of its modifications is not for routine use. A clinic might be set up, however, in some large center, where, under the direction of physicians experienced in the proper technic, selected cases could be given the advantage of this method. The part that the medical officer can play in the control of venereal disease is valuable from the standpoint of preventive medicine. Early detection and diagnosis, tracing and elimination of the source of the infection, and adequate treatment and follow-up are the keystones in the prevention of disability due to syphilis and other venereal diseases.

Chancroids may be confused with the primary lesion of syphilis. Dark-field examinations, until the diagnosis is clear, and serologic follow-up should be done to prove that syphilis was not acquired at the same time. Evidence is increasing that sulfanilamide is beneficial in many cases of chancroidal infection.^{27, 28}

In the differentiation of penile lesions, one should remember the value of skin tests—the Ito-Reinstierna test for chancroid^{29, 30} and the Frei test for lymphopathia venereum. In the treatment of the latter disease, sulfanilamide has proved of value.³¹

OTHER SKIN DISEASES OF YOUNG MEN

Numerous cases of other relatively common diseases will occur in the young men inducted into the Army or Navy as essentially healthy persons. There will be many cases of dermatitis from the many contacts made in the field or in camp. A dermatitis may appear anywhere, it may be obstinate and may cause much disability, and much detective work, to ferret out the exact causal factor, may be required. It is essential that soothing treatment be given at the beginning, or when the diagnosis is in doubt. Light³² has well outlined the therapy of acute undiagnosed manifestations on the skin.

Overtreatment was mentioned above, but it deserves emphasis again. Dermatitis from therapy, whether it is due to self-medication without a proper diagnosis, to improper medication from an error in diagnosis, to the excessive application of an appropriate remedy or to hypersensitivity of the patient, causes more visits to the dermatologist than any other single skin disease. Miller, Ayres and Alderson³³ point out that many patients seek relief because of such treatment and not because of their primary complaint. A longer period of disability

NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-FIRST ANNUAL MEETING

House of Delegates, May 11, 12 and 13

(Concluded)

After commending the committee for its excellent work, Dr. Sycamore, of the Committee on Officers' Reports, recommended that the House of Delegates express its sincere appreciation of the work of the Committee on Maternity and Infancy, and extend its congratulations to the members of this committee for their high standard of achievement; it was voted to adopt this portion of the report.

At this point, the reading of the reports was interrupted to permit a discussion by Dr. Burroughs, who spoke on the New England Institute. This is strictly an educational institute and is intended to provide some theoretical training in public health to local health officers, to the workers of various local volunteer agencies, to the staff of the state departments of health and to any others who may be interested. It is particularly valuable because many of these people have no opportunity for formal training in public health.

In the ordinary rotation, next year will be the year for the institute to come to New Hampshire. It was held in New Hampshire in 1926. From 1930-1938, it was dropped, but it was revived in 1939 in one section, and in 1940, it was fully revived, and has been held every year since then. The 1942 session has just been held in Providence, Rhode Island, with an attendance of 972 from the six states of New England.

The State Board of Health voted to recommend to the Governor and Council that this institute be held in New Hampshire in 1943; that recommendation was laid before the Governor and the Council for consideration.

At the meeting held at Hartford, Connecticut, in 1940, the Connecticut State Medical Society was one of the co-sponsors, and was responsible for one of the sectional meetings, which occupied the afternoon of one day of the institute.

Dr. Burroughs asked if, in the event that this meeting should be held in New Hampshire next year, the New Hampshire Medical Society would be interested in co-sponsoring and in putting on a sectional meeting. No expense would be entailed by the Society, because the State Board of Health would handle the cost, as well as the details, on behalf of the Secretary of the New Hampshire Medical Society.

President Dolloff asked what being a sponsor entailed.

Dr. Burroughs replied that it constituted having the name printed on the programs and officially endorsing the institute.

Dr. D. G. Smith moved that the Society be a co-sponsor of the New England Health Institute, the details of the participation of the Society to be left to the Committee on Public Health.

Dr. Metcalf stated that Dr. Burroughs had told him that the State Board of Health would be very glad to arrange the program. However, Dr. Metcalf did not know the health officials who ought to be on the program. There are three days, and the sponsor is responsible for half a day. The Board of Health, in co-operation with the Committee on Public Health, could pick out the men who are going to speak and place them on the program.

The motion presented by Dr. Smith was then seconded and carried.

Dr. Parsons asked if any delegate knew of any members of the county societies who would be interested in taking a course covering the medical aspects of chemical warfare, at either the University of Cincinnati or another teaching center.

The report of the Committee on Medical Economics was then presented.

Report of the Committee on Medical Economics

The chairman of the Committee on Medical Economics, Dr. Clarence E. Dunbar, has been called into active service with the Army Medical Corps, and the work has been carried on since his departure by the remaining two members. We have greatly missed Dr. Dunbar's wise counsel in our deliberations.

The committee has directed its attention to three major problems the first of which is a medical-service corporation.

In pursuance of the instructions received from the House of Delegates, your committee has conferred with Attorney Sulloway regarding an enabling act to permit the establishment by the New Hampshire Medical Society of a Medical-Service Corporation in New Hampshire. Attorney Sulloway has drawn up a proposed act, with due reference to the recommendations of your committee and the laws and regulations governing the operation of the insurance corporations in New Hampshire, and a copy is appended to this report. Your committee has scrutinized this act and believes that it embodies the provisions that have been

proved by experience in other states to be essential to the successful working of such a plan. We wish to commend the careful and conscientious effort that Attorney Sulloway has given to this task.

Your committee recommends that the New Hampshire Medical Society approve the proposed Act Governing Medical-Service Corporations and instruct the Committee on Public Relations to secure its introduction into the next session of the Legislature.

It is to be emphasized that the passage of the act by the Legislature would in no way obligate the Society to embark on a program of prepayment medical care but would merely establish the legal setup under which such a program could be instituted at any time in the future when such a step should seem advisable.

The work of the National Physicians' Committee for the Extension of Medical Service is of continuing importance and will be of greater value as time goes on. The trend toward governmental regulations of medical practice was gaining rapid momentum until interrupted by the war emergency. No thoughtful observer doubts that this trend will be resumed at the conclusion of the war. It will be accelerated in fact by the economic problems of the postwar period. The preservation of the personal relation between physician and patient which we believe to be the most efficient and effective form of medical care depends largely on the efforts of the medical profession to educate the public to awareness of its value. The National Physicians' Committee has proved itself an effective instrument for this purpose, and as such deserves the support of the medical profession.

The budget of the National Physicians' Committee would be met by a contribution of one dollar from each member of the American Medical Association, and this seems a small enough amount for each of us to invest in his own future. Your committee recommends that the House of Delegates request each component county society to make such a contribution to the treasurer of the New Hampshire Medical Society, to be forwarded to the National Physicians' Committee as a contribution from the physicians of New Hampshire, and that a committee of the Society be constituted to co-operate with the National Physicians' Committee in its educational work and in the securing of the necessary contributions for its support. The Committee on Public Relations might logically be designated to carry out this task.

Your committee has wrestled with the problem of compensation for the physician in service, but it believes that the more it wrestles the more it becomes enmeshed in the coils of this knotty question. It is certain that no recommendation can be formulated that will be universally applicable to every situation. In some circumstances it would be only just that part of the fees collected from the patients of a colleague who is in the service should be remitted to him. Such action must be left however to the judgment and conscience of each physician. Consideration is being given to the possibility of issuing a limited license to any physician coming into the State to take over the practice of one who has entered the service—such a license would be valid only for the duration of the emergency. Your committee has no specific recommendations to make, however, regarding this complex problem.

The Committee on Medical Economics was instructed at the last meeting of the House of Delegates to investigate the problem of medical care for low income families in rural communities. This problem however has apparently been solved by the changing economic situation and

the State Grange believe that there is no need for such an investigation at the present time.

LESLIE K. SYCAMORE *Acting Chairman*
RICHARD W. ROBINSON

Dr Sycamore moved that the Committee on Public Relations be instructed to secure the introduction of the enabling act into the next session of the Legislature.

This motion was duly seconded and was carried.

Dr Sycamore then moved the adoption of the portion of the report relating to the work of the National Physicians' Committee.

Dr Metcalf asked how this money would be turned over to the National Physicians' Committee.

Dr Sycamore replied that the treasurers of the county societies would turn it over to the treasurer of the New Hampshire Medical Society.

The motion presented by Dr Sycamore was duly seconded and carried.

Dr Sycamore then moved that the House of Delegates approve the principle of limited licensure of physicians who move to the State to replace those who enter the armed forces.

This motion was duly seconded and carried. President Dolloff presented the report of the Committee on Mental and Social Hygiene.

Report of the Committee on Mental and Social Hygiene

There have been no new developments in New Hampshire in the field of mental and social hygiene during the last year nor are there likely to be for some time to come. Specialists in the field of mental hygiene are making what contribution they can to the effort to prevent another billion dollar expense to the Government such as that resulting from the previous war because of the comparatively large number of prepsychotics and other misfits taken into the Army.

The institutions expect to take a severe setback in both their intramural and extramural activities. With the competition offered by the Federal government in munitions plants and other employing agencies the institutions can hardly be expected to retain or replace good intelligent employees who can easily obtain work at more pay and fewer hours elsewhere.

Under ordinary circumstances we should encourage early commitments but under present conditions we suggest that no one be sent to the institutions who can be cared for elsewhere.

Since the microcephalic patients usually have ossified cranial sutures at birth the officials at the State School are convinced that medical schools should prepare physicians to recognize the grosser degrees of mental defect at birth and that they should be reported to the Board of Health as such. Although notification is made of a case of measles which lasts ten days no record is made of the birth of an idiot, who is a living first mortgage on the State for life.

This state has an excellent sterilization law and if it ever approaches the subject is mentioned it should re-

main a very useful aid in our battle with mental deficiency and mental disease.

Since there is no particular connection between mental and social hygiene, and since each calls for a different line of thought and investigation, we recommend that a separate committee for social hygiene be created by the House of Delegates.

The New Hampshire Hospital Association has a committee on legislation, whose function it is to keep track of proposed legislation affecting hospitals, but there does not appear to be any similar committee of this Society.

CHARLES H. DOLLOFF, *Chairman*
BENJAMIN W. BAKER
JOHN B. MCKENNA

Dr. Sycamore stated that the Committee on Officers' Reports agreed that social hygiene is a separate field from mental hygiene, and moved that questions of social hygiene be placed under the jurisdiction of the Committee on Public Health, and that, at the next revision of the by-laws, the words "and Social" be struck from the title of this committee.

Dr. Dye asked whether the revision of the by-laws should not be referred to the Committee on Constitution and By-Laws.

Dr. Sycamore answered in the affirmative, and amended his motion accordingly.

The motion was then duly seconded and carried.

Report of the Committee on Tuberculosis

It is with deep regret that the Committee on Tuberculosis records in this report the death on January 29, 1942, of one of its members, Dr. Robert M. Deming, late superintendent of the New Hampshire State Sanatorium at Glenciff. Dr. Deming had been a member of this committee for many years. He had served the State of New Hampshire as superintendent of the sanatorium at Glenciff from 1922 until his death.

For twenty years, Dr. Deming had given unstintingly of himself in devoted service to his patients. Under his leadership and administration, the sanatorium had been developed into one of the Nation's best for the treatment and cure of tuberculous patients. He was a valiant worker in the campaign for the early detection, prevention and treatment of the disease. His death is a serious loss to the tuberculosis campaign in our state.

It is interesting that within the past few years an active campaign has been under way for the organization of tuberculosis committees in state and county medical societies throughout the Nation. Only recently, the Pennsylvania State Medical Society announced the organization of a state tuberculosis committee in its membership.

It is probably true that the New Hampshire Medical Society can claim the distinction of having organized the first tuberculosis committee in a state medical society. This committee was appointed in 1914.

Throughout the years, your committee has worked with the following objectives in view: to stimulate active interest in combating tuberculosis on the part of physicians in general practice; to establish a harmonious and helpful relation between the medical profession and official and voluntary organizations engaged in the control of tuberculosis; and to keep the profession informed concerning resources in the State for the diagnosis, preven-

tion and treatment of the disease and of progress toward its control and eradication.

The encouraging progress that has been made in combating tuberculosis in New Hampshire is due in large measure to the active support and aid of the members of the New Hampshire Medical Society.

In 1940, the tuberculosis mortality in the State fell to a new low figure of 21.2 per 100,000 population. In 1916, the death rate was 114.5. Only six states in the Nation had a lower death rate than New Hampshire—Utah, Wyoming, Iowa, Nebraska, Idaho and North Dakota. According to a statistical study made by the National Tuberculosis Association of the percentage of reduction in tuberculosis death rate among the states of the union in the period 1916 to 1940, New Hampshire presented the greatest reduction—81.5 per cent. This splendid result is due to the united effort of our physicians, sanatoriums, health and school departments, tuberculosis agencies and the people throughout the State.

As always, our problem is to find tuberculosis cases in all stages of the disease, best of all in the earliest stages and even before activity is present.

An excellent piece of tuberculosis case finding is being carried on at the Selective Service Induction Center in Manchester. An essential part of the examinations at this induction center is an x-ray examination of the chest for every man. We are not permitted to give out figures regarding the number of men called, or other statistics, but it can be stated that because of these chest x-ray examinations, tuberculosis is being kept out of our military forces and that the entire program is aiding materially in the discovery of tuberculosis in the State. All men rejected because of tuberculosis are reported to the State Board of Health, and follow-up service is provided by the New Hampshire Tuberculosis Association.

For some years, your committee has emphasized the great value of the chest x-ray film in the discovery of tuberculosis. It is known that the lesions can be seen on the chest x-ray film before signs can be heard by the stethoscope. We again urge on the members of the New Hampshire Medical Society frequent use of the chest x-ray examination. The New Hampshire Tuberculosis Association is ready to provide chest x-ray films for persons referred by physicians when these persons are unable to pay for them.

We urge prompt examination of all members of the family when a case of tuberculosis is found, since in a household where an open case has been discovered, we usually find that all members are positive tuberculin reactors.

We urge at least a tuberculin test for all persons caring for children. This should be a routine procedure for nursemaids, governesses and others in contact with children.

Bed rest continues to be emphasized in treatment. In most sanatoriums, on admission of patients, all are on bed-rest regime for study by the physicians and decision about activity of the disease.

In addition to rest treatment, various forms of chest surgery, such as pneumothorax, phrenicectomy, phrenicotomy and thoracoplasty, continue to be emphasized as aids to cure of the disease.

In this connection, it seems advisable for the best interests of the chest surgical services in our two sanatoriums that this program of treatment be developed under the direct charge and supervision of one chest surgical service.

By means of this procedure, possible chest surgical cases would be reviewed oftener and followed up more thoroughly so far as the carrying out of recommendations for treatment is concerned. Also, the responsibility would be more definitely allocated. Furthermore, in conjunction with this plan, a definite program of providing costs of treatment could be developed.

One of the members of the committee made a study this spring in Michigan of the chest surgical services in that state. The program is carried out along the lines we have suggested as being advisable in New Hampshire. In Michigan, the program has been thoroughly developed and is now in operation for some years, and appears to be working successfully.

For some time, it has appeared that the policy of restricting admissions to one of the two sanatoriums in the State to far-advanced pulmonary tuberculosis cases has not been satisfactory. Theoretically, a sound policy in practice it has resulted in lowered morale in the institution and reluctance of patients to enter it. During the past three years, in this one sanatorium 75 deaths occurred—almost half within sixty days after admission.

During the past year, the New Hampshire Tuberculosis Association has been making a study of this problem. In the summer of 1941, the association sent a questionnaire to the executive secretaries of the state tuberculosis associations of the United States asking information regarding presence of a similar problem in their respective states and how it had been solved. Forty-four states sent replies. Some few were working on the problem, all the others had had similar experiences and had solved it by dividing their states into districts or sections and by admitting patients in all stages of the disease to the sanatorium in the district or section in which they live. It is our opinion that this policy should be carried out in New Hampshire.

The New Hampshire State Sanatorium and the New Hampshire Tuberculosis Association continue to offer their services in the interpretation of chest x-ray films sent to them for diagnosis.

The Nation is engaged in a great world war. Today tuberculosis is more than a threatening shadow. It is a definite obstruction to victory, acting like sand in the gears of the production and fighting machine. Longer hours of labor and increased mental and physical strain tend to increase tuberculosis. The infection is still wide spread among our people. Tired bodies may permit ever lurking germs to attack the lungs successfully.

There must be no letup in the campaign against the disease. In fact, the fight must be carried on with ever greater aggressiveness to hold the germs won.

Your committee wishes to express its appreciation for the wholehearted assistance and encouragement accorded to it by the members of the New Hampshire Medical Society.

ROBERT B. KERR, *Chairman*
M. DAWSON TYSON

Dr. Sycamore, after commending the committee for its work, moved that the House of Delegates approve the recommendations of the Committee.

This motion was duly seconded and was carried.

Dr. Robertson read a letter from the American Medical Association Bureau of Medical Economics, addressed to the secretary of the Society, regarding H. R. 4476, now in the Senate Committee on Military Affairs. He moved that

the recommendation contained in the letter be seconded by the Society, that such notices be sent to the Committee on Military Affairs, and that a personal note be sent to Senator Bridges, who is a member of the Committee on Military Affairs.

This motion was duly seconded and carried.

Dr. Robertson then read a letter concerning the proposed tax on hospitals and colleges, which may be enacted. The tax referred to would affect the incomes of educational and charitable institutions derived from funds received from real-estate investments. Dr. Robertson stated that the Committee on Communications and Memorials recommended that the secretary of the Society be instructed to notify the congressmen and senators that the Society, as a body, protested any abridgment of the exemptions now allowed by Section 101 of the revenue laws regarding charitable and educational institutions.

This motion was duly seconded and carried.

Dr. D. G. Smith then made his report as delegate to the American Medical Association.

Report of the Delegate to the American Medical Association

The ninety-second annual session of the American Medical Association was held at Cleveland, June 2-6, 1941. It was a well attended and interesting meeting, at which your delegate served as a member of the Committee on Executive Session. The Distinguished Service Award was given to James Ewing of New York, and Fred W. Rankin of Lexington, Kentucky, was chosen president-elect. There was considerable discussion of specialty boards for the general practitioners, and there was also a demand for a new section of the scientific assembly for this group. It was decided to have an experimental session for general practitioners in the Section on Miscellaneous Topics at the next session. This is to be held at Atlantic City, June 8-12, 1942, and is to be known as the Pan American Session.

A report was made of the indictment and trial of the American Medical Association, and it was voted by the House of Delegates that the Trustees be instructed to direct counsel to appeal the judgment based on the verdict of guilty against the Association.

Medical preparedness was the chief topic of discussion at the meeting. A resolution requesting the Surgeons General of the Army and Navy to make women physicians eligible for reserve commissions was disapproved, although the spirit of American medical women in offering their services to the Government was applauded. Payment for services of the physicians serving with the Selective Service System was disapproved. A resolution was adopted requesting the establishment by the federal government of a Procurement and Assignment Agency. It was proposed that this agency should continue the work of the Medical Preparedness Committee of the American Medical Association, and that it should have authority for the selection of physicians who would be necessary for immediate duty and who would be called from civilian practice to serve with the armed forces. Such an agency has been established as known as the Procurement and Assignment Service, and is in operation at the present time. Its function is to procure physicians for the

armed forces, and at the same time to be certain that the medical needs of the civilian population are taken care of.

DEERING G. SMITH

Dr. D. G. Smith then presented the report of the Committee on Medical Preparedness.

Committee on Medical Preparedness

The Committee on Medical Preparedness has continued its co-operation with the Selective Service System and has approved all appointments of physicians as examining physicians and members of the medical advisory boards. Most of the work of this committee has been taken over by the Procurement and Assignment Service, with Dr. Deering G. Smith as state chairman; Drs. Ezra A. Jones and John P. Bowler serve with him. This service has the twofold purpose of securing physicians for the armed forces and providing for the care of the civilian population. The availability for active service of each physician in the State is to be determined. No federal appropriation of money has been made to carry on this work, although it is hoped that such an appropriation will be made in the near future. Some state medical societies are going to continue to finance the project, whereas others are planning to accept federal funds. Your committee desires the decision of the House of Delegates.

An intensive recruiting drive is about to be started in this state, to secure fifty physicians for the army before July 1, 1942. Captain E. L. Wiemers, representing the Office of the Surgeon General, and Lieutenant R. G. Vedeler, representing the Office of the Adjutant General, will be working with Dr. Smith, and it is expected that commissions will be granted within a week of the time of application.

DEERING G. SMITH, *Chairman*

EZRA A. JONES

CARLETON R. METCALF

Dr. Sycamore, acting for the Committee on Officers' Reports, recommended that the House of Delegates express to Dr. Deering G. Smith its sincere appreciation of the whole-hearted and unselfish enthusiasm with which he had devoted himself to the exacting and often thankless duties of the Procurement and Assignment Service, giving freely of his time and energy, although frequently at no inconsiderable inconvenience to himself and detriment to his own practice.

For the work of the Procurement and Assignment Service, a large number of detailed records must be kept; a great deal of correspondence is entailed, and the frequent use of the telephone and telegraph is necessary. Obviously, no budgeting of such items is possible. Dr. Sycamore therefore recommended that the Treasurer be instructed to defray all necessary expenses incident to the work of the committee, and that reimbursement be made for expenses already incurred.

After much discussion, a motion by Dr. Robertson—that the Government be allowed to pay the expenses of the Procurement and Assignment Service—was lost. Dr. Sycamore then moved that the expenses incurred by Dr. Smith be paid out of the general funds of the Society.

This motion was duly seconded by several of the members present and was carried.

Dr. Gray then spoke on the status of chiropractors in New Hampshire. He stated that at the spring meeting of the Rockingham County Medical Society, the delegates were instructed to bring before the meeting a recommendation, which was as follows:

The Rockingham County Medical Society is unalterably opposed to the practice of chiropractic. The kindest thing one can say for it is that it is quackery.

It is obvious that only by pressure politics could chiropractic have obtained a foothold in New Hampshire. It can be ousted only by pressure politics. This will mean that the Society is willing to expend money and employ legal talent to conduct a successful fight.

The delegates of Rockingham County are instructed to bring this matter before the New Hampshire Medical Society. As a Society, we favor a study of this problem, with a view to definite action in the coming legislature. We favor any legitimate action, even at considerable expense, that can bring about a revocation of chiropractic in New Hampshire.

Dr. Metcalf stated that the chiropractors usually have two or three members in the Legislature, and that the recommendation proposed would probably only make enemies and would not succeed in forcing the chiropractors out of business.

Dr. H. O. Smith then stated that the detailed report of the Trustees would be given on Wednesday afternoon, but that some financial matters should be touched on at this meeting, which was probably the most largely attended meeting of the House of Delegates. He then made the following remarks:

As most of you are aware, all the invested funds of our Society have, until last July, been deposited in various savings banks. A year ago, the Board of Trustees thought it wise to diversify our investments further, the determining factor being the strong effort then being made by the national authorities to sell savings bonds of various types.

Our purchases were of Series G bonds, a registered current income security paying $2\frac{1}{2}$ per cent a year in semiannual installments, the funds being taken from accounts and banks that seemed to us advisable.

You should know that this transfer was made without the loss of interest for a single day, and that these bonds are yielding a slightly higher rate of interest than was being paid by the banks. But, in view of present conditions, the important thing is that the New Hampshire Medical Society now has \$10,000 invested in the future of America.

Dr. Sanders then spoke as follows:

Last year, I had the honor of being elected vice-president at the meeting of the House of Delegates. Because a number of our physicians will enter the armed services, I believe that I shall be working to the limit of my strength next year; therefore, and because the last two winters have been rather trying to me, I shall not be able to assume the burden of the duties

of president of the New Hampshire Medical Society, and I do not wish to be a candidate for the office of president. This year will be a legislative year, and it is sometimes hard to get from Claremont to Concord. I believe that I should not take this office.

Dr Wilkins expressed his regret that Dr Sanders declined the office.

Dr Gray stated that an important matter brought up by the Rockingham County Medical Society was the practice by naval doctors, particularly in Portsmouth. Those men stationed at the Navy Yard are engaging in civilian practice in their hours off, and they wanted to know what their status was. Dr Gray had written a letter to the Board of Registration to see whether or not a license was required. In the Army, medical men have definite instructions not to indulge in civilian practice unless they are stationed in their own communities. That apparently was not so in the Navy, because some of the men in Portsmouth are indulging in practicing medicine. The members of the Rockingham County Medical Society wanted to know if the House of Delegates could take some action or make some recommendation.

Dr Burroughs stated that he had discussed the matter with the naval authorities about three years ago, when the present marital blood test legislation was passed. He presented the senior medical officer in Kittery with a set of applications for the Board of Registration in Medicine, for the reason that a license from the Board of Registration in Medicine is required in the people who certify for marriage purposes. The senior medical officer told Dr Burroughs that the Navy was considering following the precedent already established by the Surgeon General of the Army, namely, that medical officers of the Army were prohibited from engaging in civilian practice in the vicinity of the Army posts. No such regulation had been issued by the Surgeon General of the Navy, but it was anticipated that such a regulation might be issued, and in the meantime, the Surgeon General's policy was definitely to discourage such activity on the part of the naval officers. The medical officer returned the set of blank applications with the comment that the Navy doctors had no use for them.

Dr Burroughs further stated that the Attorney General had informally ruled that, since the Navy Yard in Kittery is actually located on the borders of New Hampshire, on the line of New Hampshire and Maine, a commission in the Navy should be regarded as having the same effect as a license in the adjoining state, hence, a naval medical officer situated at Portsmouth, holding a commission

from the Navy, should be considered authorized to practice medicine in New Hampshire, under that exception in Section 18 of the Medical Practice Act, which states that so long as he does not establish an office or appoint a place to meet patients in New Hampshire, any physician practicing on the borders of New Hampshire and duly licensed in his own jurisdiction does not require a license in New Hampshire.

Dr Gray stated that the Belknap County Medical Society requested the New Hampshire Medical Society to grant to Edwin P. Hodsdon of Lakeport, the privilege of affiliate membership with the Society, and the privilege of nonpayment of dues. Dr Hodsdon was given a gold medal for fifty years of practice at this annual meeting.

Dr H. O. Smith moved that Dr Hodsdon be made an affiliate member of the New Hampshire Medical Society.

This motion was duly seconded and was carried.

The first meeting of the House of Delegates was adjourned at 10:55 p.m.

* * *

The House of Delegates convened at the Hotel Carpenter, Manchester, on May 12, 1942, at 8:30 a.m. with Speaker Timothy F. Rock, of Nashua, presiding.

The following members answered the roll call:

The President, *ex officio*
 The Vice President, *ex officio*
 The Secretary-Treasurer, *ex officio*
 P. R. Hoyt, Laconia (alternate for Lyall A. Middleton, Plymouth)
 Emil J. Gage, Laconia (alternate for Richard W. Robinson, Laconia)
 W. J. Paul Dye, Wolfeboro
 Francis J. C. Dube, Center Ossipee
 Walter F. Taylor, Keene
 Norris H. Robertson, Keene
 Leander P. Beaudoin, Berlin
 Lewis C. Aldrich, Jefferson
 Everett C. Campbell, Woodsville
 Arthur W. Burnham, Lebanon
 Leslie K. Sycamore, Hanover
 George V. Fiske, Manchester
 Deering G. Smith, Nashua
 H. O. Smith, Hudson (appointed as alternate for Charles H. Culler, Peterborough)
 George C. Wilkins, Manchester (appointed as alternate for Clarence E. Dunbar, Manchester)
 William P. Clough, Jr., New London
 Clinton R. Mullins, Concord
 Frederick S. Gray, Portsmouth
 Anthony E. Peters, Portsmouth
 Louis C. Theobald, Exeter
 Albert E. Barcomb, Farmington
 George G. McGregor, Durham
 Bernard P. Haulbrich, Claremont
 Addison Roe, Newport

The Speaker declared a quorum present, and asked for further reports of standing committees.

Dr. Sycamore repeated the recommendations of the Committee on Medical Economics. Dr. Metcalf inquired what was meant by the words, "to replace," in the report.

Dr. Sycamore answered that, if a physician goes into a town because somebody else has gone out, such a residence is not necessarily a definite arrangement. The recommendations present one possibility of trying to protect the man who leaves his practice.

Dr. Dye stated that a ruling from the Attorney General's office concerning such limited licensure would be required. Under the present law, there is no provision for making any type of limited licensure. Dr. Dye also said that at present the Medical Practice Act requires that a man be a citizen of the United States to practice and to receive a license in New Hampshire. About the only type of person to whom a limited license could be given would be a refugee physician. In Dr. Dye's opinion, it would be very difficult and impractical to give any qualified physician a limited license to practice in New Hampshire. In other words, if a man is a graduate of a first-class medical school, having had two years preliminary education in a college approved by the Board of Registration in Medicine and one year's internship, and has passed the examinations, there would be no way of limiting his license. One disadvantageous point is that a refugee physician, if granted a limited license, might go into a community, and it is a well-known fact that every physician who practices in any community builds up a certain amount of following, so that after a year or two of practicing in that community, there would always be a group of people who would bring pressure to bear that his license be retained and that he be privileged to continue to practice there.

Dr. Sycamore stated that the Committee on Medical Economics was thinking of the refugee-physician problem, in presenting this subject for discussion. It was in an attempt to anticipate such pressure that it was deemed advisable to discuss the problem.

Dr. Wilkins asked whether this question would not finally come down to an agreement between the officials of the Procurement and Assignment Service in the State and the State Board of Registration in Medicine.

Dr. D. G. Smith was of the opinion that the resolution does not apply only to refugee physicians: there is a great possibility that it may be necessary to transplant doctors from the larger cities,—for example, from Massachusetts to New Hampshire,—to take care of some of the rural areas.

He agreed that the matter should be taken care of by the Board of Registration in Medicine, under the war emergency clause and the present statutes. He believed that the committee's idea was to obtain an opinion from the House of Delegates regarding whether or not they would approve limited licensure; such a statement would help the Board of Registration in Medicine somewhat in solving this problem.

Dr. Metcalf asked how, under the present law, a limited license could be issued.

Dr. D. G. Smith replied that the Board of Registration in Medicine would practically dictate it, under a war clause. He pointed to a section in the by-laws that requires applicants for examination for licensure to meet certain conditions: two years of premedical training, graduation from an approved school, a year's internship, citizenship and so on; the last part of that section reads: "The provisions of this section may be suspended in whole or in part by order of the Board on account of war or other threatened or existing national calamity."

So that, in the final analysis, the Board may license anybody it wishes to license. The position of the Board up to the present time has been not to let down the bars in any particular case—so far as letting in men from substandard schools and men who have not had any premedical education is concerned.

Dr. Taylor moved that the House of Delegates approve the limited license, in principle.

This motion was duly seconded and was carried, with one dissenting vote.

Dr. Dye, reporting for the Committee on Amendments to the Constitution and By-Laws, stated that various matters, largely of a technical nature, were referred to the committee. It was recommended that Chapter VIII, Section 6, of the by-laws be amended to read in full as follows: "Section 6. The Committee on Medical Economics shall consist of three members." Previously, this particular section read: "Section 6. The Committee on Medical Economics shall consist of three members, one of whom shall be elected annually for a term of three years."

This change was suggested to make it a standing committee and not a rotating committee.

Dr. Dye moved the adoption of the proposed change.

This motion was duly seconded and was carried.

Further changes recommended were as follows:

We recommend that Chapter VIII, Section 10, be amended to read as follows: "The Committee on Mental Hygiene shall consist of three members, whose duties shall be to study this special subject, co-operate as far as possible with the heads of the state institu-

tions under medical supervision and report to the society."

The only change is in the striking out of the words "Social Hygiene" and changing the plural to the singular.

I move the adoption of this amendment to the by-laws, regarding Section 10 of Chapter VIII.

In Section 12, it was a technical matter, to make this a standing committee instead of a rotating committee.

We recommend that this section be amended to read as follows: "The Committee on Medical Education and Hospitals shall consist of three members."

I recommend and I move a change in the heading of Section 1, Chapter VIII, naming one Committee as the Committee on Mental Hygiene, omitting "and Social."

With reference to Chapter I, Section 5, regarding membership, this matter was brought up because Dr. Hodsdon, who was a member of the New Hampshire Medical Society, without being a member of a component medical society, became a member prior to the formation of the county societies and now wishes to be made an affiliate member.

I should like to read the proposed amendment to Section 5 completely, as follows: "Any physician who has been a member of this Society for a continuous term of fifteen years and is either not less than sixty-five years of age or totally disabled, on personal application or on the request of his county society, may be made an affiliate member by a majority vote of the House of Delegates. Affiliate members shall have the same rights and privileges as other members of the Society, but shall not be required to pay dues."

Unless some one has any other particular question in mind regarding members, that completes our report on amendments to the by-laws.

We were asked to give an opinion regarding the clarification of the membership qualifications. I shall first read Section 2, of Article IV, of the Constitution, which has to do with the composition of the society: "The members of the Society shall be the members of the component county medical societies and the present members of the New Hampshire Medical Society."

In the first place, there is no specification that residence in New Hampshire is necessary for membership. Secondly, men who were not previously members of the Society prior to the formation of the county medical societies must now be members of a component county medical society before being accepted by the State Society.

Dr. Sanders, referring to the question of eligibility to membership in a county medical society, stated that Dr. Amsden, of Ackworth, had come to New Hampshire from New York and had applied for membership in the New Hampshire Medical Society. He continued:

I found, in looking up the matter, that it was required that a member be licensed in New Hampshire and that he be in active practice. Those requirements, I think, come through the constitution and by-laws that each county society is supposed to adopt on recommendation of the New Hampshire Medical Society.

I wondered if that was the regular practice of county societies in admitting members to the county membership—that is, a man could not merely reside, and not be in active practice or licensed, in the State, and still be a member of a county medical society.

Dr. Amsden took out a New Hampshire license, and is in practice in the State. He is a retired psychiatrist, and I think perhaps did not intend to practice in the State; however, he is practicing somewhat to keep up his membership in the American Medical Association. He gave up his New York State membership, and had to have some county membership to keep up the American Medical Association membership.

Dr. D. G. Smith moved that Article XII be deleted from the Constitution, explaining that such an action must be proposed at one annual session and then acted on at the succeeding annual session.

This motion was duly seconded and was carried.

Dr. Wilkins moved that Article XIII of the Constitution be made Article XII.

This motion was duly seconded and was carried.

Dr. Dye moved that since the by-laws had been amended to the effect that a present member of the Society may apply for affiliate membership, Dr. Hodsdon, who had written to the Society, be made an affiliate member of the New Hampshire Medical Society.

This motion was duly seconded and was carried.

Dr. Dye stated that this was not in the nature of a motion and that the delegates might want to discuss the question. He referred to Dr. J. Dellinger Barney, who had relinquished his residence in New Hampshire and wondered what his membership status would be. So far as the committee could determine, he could follow one of two courses. If his county society retained his membership, Dr. Barney could continue to be a member of the Society, since there is no provision in the constitution of the Society that a man must be a resident of the State to be a member of the Society. Should he not continue as a member of his county society, by virtue of the local county constitution, under Section 4, Article IV, he could be proposed by the House of Delegates as an honorary member of the Society.

Dr. D. G. Smith cautioned the Committee on Constitution and By-Laws to be sure that it did not conflict with the constitution of the Cheshire County Medical Society and with the constitution and by-laws of the American Medical Association, since he believed that such a conflict might occur:

The model constitution of the county society says that a doctor, to be eligible for membership, must reside and practice in the county in which he is applying for membership, with the exception that men on county lines and state lines in adjoining counties or states can belong to that county society.

Dr. Robertson inquired about members who practice in New Hampshire and are members in Massachusetts and have kept up their Massachusetts membership through the years.

Dr. D. G. Smith answered that, strictly speaking, such members can belong only to one county and one state medical society.

Dr. Sycamore said that there should be a general ruling that would cover these cases and that, in his opinion, a simpler solution would be to make them honorary members; the question of a conflict with the American Medical Association rulings would then be avoided.

Dr. Dye moved that any physician who is not a resident of New Hampshire have his individual status regarding membership in the New Hampshire Medical Society, subject to the recommendation of his component county medical society.

Dr. Sycamore asked if the American Medical Association or the component societies had the final authority.

Dr. Rock declared that he did not know who had the final authority.

Dr. Dye stated that, apparently, certain members of the House of Delegates wanted a ruling regarding cases like that of Dr. Barney, and that he had therefore moved that each county society decide the matter.

Dr. D. G. Smith stated that the question involved a double representation: a man belongs to one county society, and his membership counts as a quota toward the state society in electing a delegate; the same thing would be true if he belonged to two county societies in the State. His name would be added to their membership lists, making a quota for the members necessary to have an additional delegate to the House of Delegates. In the American Medical Association, he is listed in two different states; therefore, he contributes to New Hampshire's quota for a delegate and he contributes to the Massachusetts quota.

After further discussion, the motion previously made by Dr. Dye was seconded by Dr. Fiske and was carried.

The second meeting of the House of Delegates was adjourned at 10 a.m.

* * *

The House of Delegates convened at the Hotel Carpenter, Manchester, on May 13, 1942, at 8:30 a.m., with Speaker Timothy F. Rock, of Nashua, presiding.

The following members answered the roll call:

The President, *ex-officio*

The Vice-President, *ex-officio*

The Secretary-Treasurer, *ex-officio*

Earl J. Gage, Laconia (alternate for Richard W. Robinson, Laconia)

W. J. Paul Dye, Wolfeboro

Francis J. C. Dube, Center Ossipee

Lewis C. Aldrich, Jefferson

Everett C. Campbell, Woodsville

George V. Fiske, Manchester

Deering G. Smith, Nashua

H. O. Smith, Hudson (appointed as alternate for Charles H. Cutler, Peterborough)

George G. Wilkins, Manchester (appointed as alternate for Clarence E. Dunbar, Manchester)

William P. Clough, Jr., New London

Frederick S. Gray, Portsmouth

Albert E. Barcomb, Farmington

Bernard P. Haubrich, Claremont

Addison Roe, Newport

Dr. Dye reported for the Committee on Nominations, as follows:

OFFICERS

President: Timothy F. Rock, Park R. Hoyt and Arthur W. Burnham.

Vice-President: Ralph W. Tuttle, James W. Jameson and Fred Fernald.

Councilor for Coos County (five-year term): Richard E. Wilder.

Councilor for Carroll County (five-year term): W. J. Paul Dye.

Trustee emeritus: Henry O. Smith.

Trustee for three years: Clarence O. Coburn.

House of Delegates: speaker, Charles H. Parsons; vice-speaker, George F. Dwinell.

Necrologist: Henry H. Amsden.

Delegate (American Medical Association): Deering G. Smith.

Alternate Delegate (American Medical Association): Emery M. Fitch.

Delegates to New England Societies (1942):

Maine: Leopold T. Togus, Lawrence R. Hazzard.

Vermont: Harry B. Carpenter.

Massachusetts: Wallis D. Walker, W. J. Paul Dye.

Rhode Island: Reginald F. DeWitt, Ellsworth M. Tracy.

Connecticut: John F. Gile, James E. Bovaird.

STANDING COMMITTEES

Amendments to Constitution and By-Laws: James B. Woodman, W. J. Paul Dye, Frederick S. Gray.

Child Health: Colin C. Stewart, Jr., Travis P. Burroughs, Franklin N. Rogers.

Control of Cancer: George C. Wilkins, Ralph E. Miller, George F. Dwinell.

Maternity and Infancy Robert O Blood, Benjamin P Burpee, Marion Fairfield.

Medical Economics Leslie K Sycamore, Richard W Robinson, Francis J C Dube

Medical Education and Hospitals John P Bowler James W Jameson, Herbert L Taylor

Mental Hygiene Charles H Dolloff, Benjamin W Baker, John B McKenna

Public Health Travis P Burroughs, Anthony E Peters, Harris E Powers

Public Relations The President, The Vice President The Secretary Treasurer, Robert J Graves, Ezra A Jones

Publication Carleton R Metcalf, John F Gile, Emery M Fitch

Scientific Work Carleton R Metcalf Frederick P Scribner, Sven Gundersen

Tuberculosis Robert B Kerr, M Dawson Tyson, Clarence O Coburn

Medical Preparedness Deering G Smith Ezra A Jones, Carleton R Metcalf

The report was accepted Dr Timothy F Roel of Nashua, was elected president

Dr James W Jameson, of Concord, was elected vice president

Dr Dye, for the Committee on Nominations, recommended a standing vote on one other nomination on the slate—for trustee emeritus, Dr Henry O Smith, of Hudson

The Secretary was instructed to cast one vote for Dr Henry O Smith as trustee emeritus, this was done, and he was declared duly elected

The Secretary was instructed to cast one ballot for the remainder of officers and committee members as nominated, this was done, and all were declared duly elected

Dr Metcalf moved a vote of gratitude to the members in Manchester who had arranged the details of the meeting, it was so voted

Dr Wilkins then presented the report of the Committee on the Control of Cancer

Report of the Committee on the Control of Cancer

The Committee on the Control of Cancer has sent to every physician in New Hampshire the usual three letters of information regarding specific phases of cancer diagnosis or treatment. The first letter was devoted to prostatic carcinoma, a condition more frequently found than is generally realized, the second briefly discussed diagnosis and treatment of cancer of the mouth and the last called attention to the valuable lay educational work performed by the Women's Field Army, stressed the value of urging people to have periodic physical examinations and urged more education of the public in recognizing the significance of irregular uterine bleeding as

well as the urgency for immediate thorough examination in the event of rectal bleeding. Too many physicians are still too reluctant in carrying out the necessary examinations required to determine the cause of bleeding in these two conditions

During the year, requests for full sets of these letters, sent since 1934 to New Hampshire physicians, have been received from cancer committees in Maine, Vermont, Kansas and Georgia, and from the American Society for the Control of Cancer

In 1935, at the request of the Cancer Commission, the State Board of Health made cancer a reportable disease. The physicians of the State and the hospitals were appealed to by both the commission and the Board of Health to report all cases of cancer coming to their attention. The Pathological Laboratory at Hanover co-operated to the extent of mailing to physicians a partly filled out form with each positive cancer report. In 1941, the Board of Health at the suggestion of the commission, repealed this law because, during the six years that cancer was reportable it was found that there were reported only about 50 per cent as many cancer cases as there were cancer deaths and the reported cases came almost entirely from the cancer clinics. The Cancer Commission suggested this repeal because it seemed fruitless to continue an effort when such a lack of co-operation on the part of physicians was evidenced. Without full co-operation, there is no way of ascertaining how many active cancer cases there are in the State.

The diagnostic clinics and treatment centers supervised by the Cancer Commission have continued their excellent work, and about sixty members of the New Hampshire Medical Society are regularly taking active part in this clinic service. There is still much evidence of ignorance, apathy and delay on the part of patients in spite of the efforts of the medical profession and the widespread distribution of small pamphlets carried each year into every city, town and village by the Women's Field Army. Last year, ninety-five thousand pieces of literature were distributed and the New Hampshire leaflets are now printed in English, French, Polish and Greek. We urge all physicians of the State to read the reference book on cancer, which was sent to every physician in the State in 1940 by the Women's Field Army.

In Massachusetts the intensive cancer control campaign took ten years of constant effort before the mortality rate dropped definitely downward. The New Hampshire program is now in its seventh year, and we hope soon to observe tangible evidence of the effectiveness of medical and lay education combined with improved surgical and radiologic treatment.

Much credit should go to the alertness of the majority of the physicians in the State for their keenness and ability in recognizing cancer early and inducing patients to seek early treatment. A minority of physicians unfortunately still have a lackadaisical attitude toward thorough and adequate physical examination, early indications of cancer and the methods of making early diagnosis. These men need education but they are probably the ones who throw our letters into the wastebasket unread.

Your committee has spent \$44.35 for printing, stationery and postage in sending out nearly two thousand letters, the balance of \$5.65 having been returned to the treasurer. We request an appropriation of \$50.00 for the coming year.

GEORGE C. WILKINS, *Chairman*
HOWARD N. KINGSFORD
GEORGE I. DWINELL

Dr. Sycamore, for the Committee on Officers' Reports, recommended that the requested appropriation of \$50.00 be approved.

This motion was duly seconded and was carried.

The report of the Committee on Medical Education and Hospitals was then presented.

Report of the Committee on Medical Education and Hospitals

POSTGRADUATE MEDICAL EDUCATION

The fifth annual meeting of the Associated State Postgraduate Committees was held in Cleveland in 1941 in conjunction with the meeting of the American Medical Association. The meeting of this committee was attended by Dr. Deering G. Smith as our representative. The new chairman is Dr. Frank R. Ober, of Boston. The New England member of the Executive Committee is Dr. Frederick T. Hill, of Waterville, Maine.

This committee has been working for some five years in the attempt to co-ordinate the activities of the various state committees on medical education and hospitals, and the program being assumed by them is a steadily more pretentious one. In this connection, at their last meeting, it was voted that an assessment of \$50.00 be made against each state to provide funds for the activities of this committee. It is the opinion of Dr. Smith, who attended this meeting, and of several others, that the activities of postgraduate education in the State are too limited and will without doubt be more limited in the near future to warrant this expenditure by the Society at this time. This reason leaves out altogether the question whether or not such assessment should be on the basis of population rather than a fixed, uniform figure. It is therefore the belief of this committee that the State assessment be not recommended to the Society at this particular time.

COMMONWEALTH FUND FELLOWSHIPS

A year ago, we rendered a brief review of the activities of the Commonwealth Fund Fellowships in this state for the preceding five years through which they had been operating. It is to be expected under present conditions that there has been less interest in this activity this year as measured by the response to the circularization of the

membership of the New Hampshire Medical Society. To date, there have been requests for application blanks from only eight members of the Society, and appointments have not yet been announced by the Commonwealth Fund.

There seems to be little more that can be done in the way of calling the attention of the membership to these fellowships, which seem to be so generous and intelligent in their conception, and it is to be hoped that their value will not be lost sight of in the exigencies of the times in which we are now living.

JOHN P. BOWLER, *Chairman*
JAMES W. JAMESON
HERBERT L. TAYLOR

Dr. Amsden read the report of the necrologist.

Report of the Necrologist

The following deaths have occurred since the last annual meeting:

NAME	ADDRESS	DATE DECEASED
Abbott, Charles B.	Penacook	March 24, 1941
Cheever, Nathaniel F.	Greenfield	June 15, 1941
Cobb, Joseph J.	Berlin	July 15, 1941
Daudelin, Alfred	Nashua	September 21, 1941
Deming, Robert M.	Glenclyff	January 28, 1942
Hinds, Wm. H. W., Jr.	Milford	March 10, 1942
Kittredge, Frank E.	Nashua	July 8, 1941
LaFrance, Albert J.	Laconia	March 12, 1942
Lamb, Zenas F.	Keene	April 28, 1941
Marks, Homer H.	Berlin	April 11, 1941
Noyes, Walter F.	Colebrook	May 24, 1941
Potvin, Victor E.	Claremont	December 10, 1941
Sanborn, Benjamin E.	Manchester	October 3, 1941
Webber, Norman B.	Manchester	February 22, 1942
Weinberg, Philip B.	Whitefield	August 27, 1941

HENRY H. AMSDEN

Dr. Rock expressed appreciation to the members of the House of Delegates for their assistance in carrying on these meetings.

The third and final meeting of the House of Delegates was adjourned at 9:20 a.m.

CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28341

PRESENTATION OF CASE

A fifty-year-old man was admitted to the hospital because of cough and fever.

During the week prior to admission, the patient suffered with a "head and chest" cold characterized by a great deal of coughing productive of small amounts (not over a teaspoonful a day) of whitish sputum. He was seen by his physician on the evening prior to entering the hospital. At this time, he was coughing and vomiting, and there was some right-lower-quadrant pain associated with the bouts of coughing. There was no hemoptysis, and no chills or chest pain. Rales were audible at the posterior base of the left lung, and a murmur, believed to be early diastolic, was heard at the apex. A urine specimen was said to have contained many blood cells and much albumin.

The family history was irrelevant.

The past history was unremarkable except for an accident that occurred one year previously, when the patient fell from a truck and sustained a fractured skull. He was unconscious for twelve days, and since then he had suffered with severe left frontal headaches, dizziness and tinnitus.

Physical examination revealed a well-developed man in no distress who coughed frequently, bringing up a thin, white sputum. The chest was barrel shaped. Examination of the heart was negative, although one observer reported a systolic murmur audible to the left of the sternum and a sharp pulmonic sound. There was some impairment of resonance at both lung bases posteriorly. The percussion note was hyperresonant, with some dullness over the left lower lobe posteriorly. Sticky rales were audible in the left chest, most marked at the bases. A few persistent inspiratory rales were audible in the left infraclavicular region anteriorly. There was deep tenderness in the right upper quadrant, but no abdominal masses were felt. There was also left costovertebral tenderness. There was prominent clubbing of the fingers.

The blood pressure was 138 systolic, 80 diastolic. The temperature was 100.6°F, the pulse 96 and the respirations 24.

Examination of the blood revealed a hemoglobin of 107 gm., and a white-cell count of 8600 with

67 per cent polymorphonuclears, 5 per cent large lymphocytes, 12 per cent small lymphocytes and 16 per cent monocytes. The blood Hinton test was reported doubtful and, when repeated, was unsatisfactory. The nonprotein nitrogen was 60 mg per 100 cc. Examination of the urine revealed a specific gravity of 1.012, a +++ test for albumin and 100 red blood cells, 10 white blood cells and 10 epithelial cells per high power field. No acid fast bacilli or other pathogenic organisms were found in the sputum. A blood culture was negative.

X-ray examination of the chest showed symmetrical and diffuse linear and hazy density of both lungs, more marked at the bases. Both lung roots were enlarged, and the right side of the supracardiac shadow was moderately prominent. The heart was not definitely enlarged but was triangular—prominent across the base. The costophrenic angles were hazy, particularly in the posterior portion.

The patient complained of fever and sweating during the entire period of hospitalization. There was no chest pain, and no change in the amount of coughing. Repeated urinary examinations revealed a persistently low specific gravity, a +++ test for albumin, rare hyaline and cellular casts, many white blood cells and large numbers of red blood cells. The urine cultures revealed no growth.

Intravenous pyelograms showed no excretion of the dye. Small areas of dense calcification were found in the region of the upper pole of the right kidney. There were small flecks of calcification in the right pelvis close to the sacroiliac joint. The kidneys were normal in size and shape. The liver edge was lower than normal, and a soft-tissue mass, apparently the spleen, overlay the upper pole of the left kidney.

On the fifth day, there was less moisture in the lungs. The nonprotein nitrogen had risen to 111 mg. per 100 cc. two days later. On the ninth hospital day, while reaching for a bedpan, the patient suddenly noted pain in the right hand. The hand became cold, and the patient could not dorsiflex it. No brachial or radial pulse was felt; there were faint arterial pulsations in the axilla. On the following day, the pain was somewhat relieved. The radial pulse gradually returned. The blood pressure on this day was 82 systolic, 72 diastolic, in the right arm and 130 systolic, 70 diastolic, in the left.

A Congo red test revealed 70 per cent retention of the dye in the serum after an hour.

On the thirteenth day, the spleen was felt two or three fingerbreadths below the costal margin. The strength in the right hand had improved considerably. An x-ray film of the chest showed

little change. The diffuse, hazy density appeared to have cleared slightly.

Two and a half weeks after admission, the patient complained of slight pain in the left shoulder, which became progressively worse, particularly when he took a deep breath. A faint rub synchronous with the heart beat was audible over the entire precordium. The heart sounds were distant, but the radial pulse was regular and strong. The blood pressure was 140 systolic, 85 diastolic. That evening while on a bedpan, the patient suddenly began to breathe stertorously and expired.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON: It seems very clear to me that this patient had a bacterial endocarditis, that he had multiple emboli with infarcts, and that he had some type of renal failure, all of which led to sudden death. The questions to be answered are: What type of endocarditis was it? What type of renal failure? What was the cause of the apparent pericarditis? What was the immediate cause of death? I should like to have Dr. Hampton tell me, if he will or can, whether the x-ray film of the heart shows any suggestion of previous long-standing heart disease, perhaps congenital heart disease or some other type.

DR. AUBREY O. HAMPTON: I think the heart is definitely enlarged. It is triangular and the curve of the right auricle is high. The aorta is small, and the pulmonary vessels are dilated. The thing that bothers me most is whether there are also enlarged lymph nodes at both lung roots aside from the dilated pulmonary vessels. The heart has more the appearance of mitral disease than congenital heart disease. There is no fluoroscopic note of how large the left auricle was. This is the lateral view, but there is no oblique view, which would help more than the lateral. This shadow to the right of the mediastinum is longer and lower than the usual azygos node that one sees in sarcoid and lymphoma. It could be the vena cava, I suppose, but there must be something in addition to the vena cava there. When one sees the enlarged spleen, one wonders if these enlarged nodes are associated with that—provided they are enlarged nodes. I am not too happy about it. There is also what appears to be edema of the lung and, in addition, diffuse linear density in the lung, which could be connected with enlarged lymph nodes, as in sarcoid. I think that there was a definite heart lesion, and that there probably were enlarged lymph nodes.

DR. RICHARDSON: What about this?

DR. HAMPTON: That is a focus of calcification, but I do not know where it is.

DR. RICHARDSON: I was not paying too much attention to it.

DR. HAMPTON: It shifts in relation to the kidney cortex. Here it is about 2.5 cm. from the margin, and there is 1.5 cm. I assume that it is outside the kidney. It could be in the gall bladder, but it does not look like either gallstone or renal stone. The kidneys show very poor function. This is a 30-minute film with intravenous dye, and as you see, there is nothing in the bladder. The right kidney is low, and the edge of the liver is not so low as the edge of the spleen.

DR. HARWOOD: Could the heart shadow be simple dilatation?

DR. HAMPTON: I do not believe so. It has an abnormal shape. Simple dilatation would maintain a normal shape, I think.

DR. RICHARDSON: I shall disregard the calcification, which is a dangerous thing to do with all these calcium experts around. There is x-ray evidence that there may have been a preceding heart lesion, and the picture is somewhat suggestive of the possibility of mitral stenosis, if I understand Dr. Hampton correctly. That would give at least a background for subacute bacterial endocarditis. I was prepared to make this diagnosis in the absence of evidence of preceding heart disease because I thought that the picture was very clear. Assuming for the moment that I am right about it, if this was bacterial endocarditis, what organism was involved? It seems to me that one of the acute types—a beta-hemolytic streptococcus or pneumococcus—would have grown out in a culture. If the blood picture is correctly reported, the presence of an increased number of monocytes without a definite polymorphonuclear formula is suggestive that this was not an acute type, but more likely one due to the alpha-hemolytic streptococcus. I believe that this patient had bacterial endocarditis, with vegetations on the valves infected by the *Streptococcus viridans*.

So far as the type of renal failure is concerned, we know, accepting that diagnosis, that nephritis is a common complication of bacterial endocarditis, and I believe something like 90 per cent are glomerular and 10 per cent embolic; therefore, one ought to be in favor of the glomerular type. However, certain things lead me to suspect that the patient had embolic nephritis, or even large renal infarcts. One is that he had costovertebral tenderness, which is not very definite evidence. Another is that he had evidence of emboli in the systemic circulation. There was an embolus in the blood vessels of the arm, and it seems to me that there was enough suggestion of emboli for embolic nephritis to be considered; it is even quite possible that the patient had large renal infarcts. I therefore think that is so, and that he had uremia. I believe the uremia caused the pericardial friction rub. I do not know about that sequence of

events. I suppose that pericarditis can be associated with reactivation of rheumatic heart disease, but I think one might reasonably see that this patient had uremic pericarditis.

The cause of death seems to me most likely embolic, and since many of the embolic phenomena have been in the systemic circulation, it seems more likely that the patient had a cerebral embolus than a pulmonary embolus. I wondered whether this could have been some type of cancer and whether all these phenomena were due to cardiac invasion, possibly with the production of thrombus and embolus. There is a great deal going on in the chest that Dr. Hampton does not like. I do not like it either, but I shall not change my original diagnosis on the basis of the x-ray films. I shall say that there was not any type of malignant tumor. I do not know what the calcification was. If the patient had had a previous infarct, he might have had calcium in the infarct. In bacterial endocarditis, infarction is very common. One would expect infarcts in many organs especially the lungs, spleen and kidneys, and peripheral infarcts elsewhere. Therefore, I make a diagnosis of subacute bacterial endocarditis, probably engrafted on chronic rheumatic heart disease, alpha-hemolytic streptococcus infection and embolic nephritis, probably with large renal infarcts, uremic pericarditis, and a large cerebral embolus as the immediate cause of death.

DR. FULLER ALBRIGHT: Are you disturbed that the kidneys were small? They are usually not small with large fresh infarcts.

DR. RICHARDSON: I think it is very reasonable. I think there was endocarditis for some time before the three weeks mentioned in the history.

DR. ALBRIGHT: How about the sterile urine? Embolic nephritis is not associated with sterile urine.

DR. RICHARDSON: I do not know. I do not believe that is necessarily true.

DR. ALBRIGHT: I do not know that it is, either, as a matter of fact.

DR. F. DENNETTE ADAMS: Why do you think that a large cerebral embolus, rather than a pulmonary embolus, accounted for this very sudden death? Do you not expect cerebral hemorrhage to last a few hours?

DR. RICHARDSON: Yes; my reasoning was that there was one in the arm, and it seemed more on the systemic than the pulmonary side. Accordingly, I put it there. I thought the description was not quite that of ordinary pulmonary embolism, but there is really nothing to go on.

DR. MAURICE FLEMING-SMITH: Is the x-ray film consistent with pericardial fluid?

DR. HAMPTON: With the exception of the lung roots, yes. If the patient had perfectly normal lungs and pulmonary vascular shadows, it would

be quite consistent with it, but apparently he had something going on in the pulmonary vascular system for a long time before that. The heart is not very large, so that the whole thing can be explained by mitral stenosis.

DR. ALBRIGHT: You do not know the calcium and serum protein?

DR. TRACY B. MALLORY: No.

DR. HAMPTON: Another thing—the chest films were not taken at the time he had pericardial symptoms.

DR. WILLIAM BISHOP: I should like to comment about the head injury a year previously. I saw the patient outside the hospital for quite a long time because of that trouble, and had a chance to examine him repeatedly. I sent him to Dr. John S. Hodgson, with the question of whether he had residual hematoma following the head injury and fracture, but we could not make out that there were any definite signs. He had no good localizing evidence of any really organic cerebral damage, but it seemed to me as I observed him that he was slower mentally than originally, although he was never very brilliant, and it was difficult to be sure of that. He was asked whether or not he felt able to go to work. At times, he thought he could, and at other times that he could not; but he never did return to any occupation. His chief complaints up to the time of the last illness were headache and dizziness, dizziness especially on looking up too quickly. I saw him just before admission to the hospital, and the heart murmur, rales and especially the markedly bloody urine were the things that led me to urge him to come to the hospital. I was more or less jockeyed out of my impression that he had a heart murmur. Some heard it, and some did not. Then I changed my mind and said it was a systolic murmur. Now I should like to think I really heard a diastolic murmur. I knew that there must have been something abnormal in the heart that was giving rise to emboli, perhaps a mural thrombus. I did not come to a definite conclusion that he had bacterial endocarditis.

DR. FLETCHER H. COLBY: I saw the man mainly because of the hematuria. The gross hematuria in conjunction with the high nonprotein nitrogen and lack of excretion of dye in the intravenous pyelogram suggested some sort of nephritis. On the other hand, when I first saw him the nonprotein nitrogen was 50 or 60 mg per 100 cc, and we planned to cystoscope him to see if we could discover some source of bleeding, such as a bladder tumor. He quickly got too ill, and we canceled arrangements. That was the time of the embolus to the axillary artery. The spleen was easily felt when he first came in. That was not brought out in the history.

CLINICAL DIAGNOSES

Acute glomerulonephritis.
Uremia.

DR. RICHARDSON'S DIAGNOSES

Subacute bacterial endocarditis (alpha-hemolytic streptococcus), probably secondary to chronic rheumatic heart disease.
Embolic nephritis, with large renal infarcts.
Uremic pericarditis.
Cerebral embolus.
Multiple infarcts.

ANATOMICAL DIAGNOSES

Endocarditis, subacute bacterial, mitral.
Endocarditis, chronic rheumatic, mitral, with stenosis, and aortic, with interadherence of cusps.
Cardiac hypertrophy, moderate.
Pericarditis, serofibrinous, early.
Subacute glomerular nephritis.
Pulmonary hemorrhage, bilateral, interstitial, focal.
Splenic infarction.
Embolism of brachial artery, with extension into subcapsular artery.
Encephalomalacia, localized, bilateral, post-traumatic (head injury).
Hypertrophic pulmonary osteoarthropathy.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Post-mortem examination showed bacterial vegetations on the mitral valve, superimposed on a well-marked calcareous rheumatic stenosis. There had been numerous emboli from this source. We located the one in the brachial artery, and found two small infarcts in the spleen and two in the kidney. The kidneys were very large, weighing 600 gm. The cortices were markedly swollen, and the surfaces were smooth but covered with petechial hemorrhages. There has been quite a little discussion of the question of embolic nephritis, and I think the clinicians today have used the term in a sense that is distinctly different from the usage of most pathologists. In the average case of bacterial endocarditis, one finds some changes in the glomeruli, and patients have during life, at least at times, hematuria. The ordinary case of bacterial endocarditis, however, shows these glomerular changes only in isolated glomeruli, whereas the majority of the glomeruli remain normal. Moreover, even an involved glomerulus may show inflammatory changes limited to only a portion of the tuft, the other loops of the tuft remaining perfectly normal. Consequently, most of the patients have good renal function, and a uremic death is rare. Because this type of glomeru-

lar disease occurs so regularly in bacterial endocarditis, it has often been called "embolic nephritis." There is really in most cases no direct evidence that it is embolic, and the same lesion is frequently found in acute disseminated lupus without endocarditis or other focus from which embolism could arise. Therefore, the term "focal glomerular nephritis" is preferable. I think what Dr. Richardson and Dr. Albright have been referring to is true demonstrable embolism to the kidney. This may be so massive, or miliary emboli may be so numerous, that renal insufficiency develops. Such cases are, however, rare. In this case, the microscopic sections showed a true diffuse glomerular nephritis indistinguishable from a primary glomerulonephritis. All glomeruli were involved more or less uniformly and completely, so that the development of renal insufficiency is not surprising.

There were one or two other findings of interest. The myocardium showed very obvious fibrous scarring in scattered spots throughout the heart. The aorta and coronary arteries, however, were practically free from sclerosis, and there was no evidence of any emboli to the coronary arteries. Later, on microscopic examination, it was apparent that these spots of fibrosis in the myocardium were all extremely old. There were no signs of any fresh myocardial necrosis, and no trace of inflammatory reaction in any of these scars. Consequently, this myocarditis must be put far into the past history, perhaps back to the time when the patient acquired the mitral stenosis, and hence may well have been of rheumatic origin. It is also conceivable that he had had diphtheria unknown to us in the past, which is the commonest source of that sort of lesion. The brain did show definite evidence of damage from the accident a year before. There were foci of superficial cortical atrophy, with marked hemosiderosis of the overlying arachnoid.

DR. HAMPTON: Sudden death was due to what?

DR. MALLORY: It was due to no cause that we could discover. There was massive acute pulmonary hemorrhage, or edema—very hemorrhagic serosanguineous fluid. The heart weighed 500 gm., and there was no atheroma of either the pulmonary or the coronary arteries.

CASE 28342

PRESENTATION OF CASE

A seventy-year-old man was admitted to the hospital because of persistent hematuria.

Three months before admission, the patient slipped while walking and twisted his right side. Following this, he had slight pain and an ache in the right flank that disappeared after several days.

At that time, he noticed the onset of hematuria, persistent to the day of admission except for a single period of three weeks. The degree of hematuria varied considerably and occurred during all parts of micturition. There was no dribbling, hesitancy or incontinence. A slight burning occasionally accompanied urination, and the patient occasionally suffered with nocturia and frequency.

Two months prior to admission, he was cystoscoped in the Out Patient Department and found to have a papillary growth of the bladder 1.5 cm. above the left ureteral orifice.

For three weeks before admission, the patient had an uncomfortable feeling in the left groin, and three days prior to entry he suffered with low midback pain lasting a day.

The past and family histories were irrelevant.

Physical examination revealed a well-preserved elderly man in no distress. Examination of the lungs and heart was negative except for a systolic murmur at the apex and over the aortic area. The abdomen was soft, and no masses were felt.

The blood pressure was 150 systolic, 92 diastolic. The temperature, pulse and respirations were normal.

The urine showed a +++ test for albumin, a few white blood cells and many red blood cells. There were no casts, and the concentration was good. A culture of the urine revealed a few colonies of *Staphylococcus albus*. Examination of the blood showed a red-cell count of 4,250,000 with 75 per cent hemoglobin, and a white-cell count of 6300 with a normal differential. The nonprotein nitrogen was 23 mg. per 100 cc., and the prothrombin was normal. The phenolsulfonephthalein test showed 35 per cent excretion in fifteen minutes, and an additional 15 per cent in half an hour. X-ray films of the skull and chest revealed no lesions resembling metastases.

Cystoscopy failed to reveal the papillary growth of the bladder previously seen in the Out Patient Department. An intravenous pyelogram showed delayed excretion of the dye, which faintly outlined the ureters and kidneys. The bladder outline was relatively smooth; there was a slight defect at the base consistent with an enlarged prostate. A retrograde pyelogram demonstrated bilateral pressure defects along the upper surfaces of both kidneys. However, the lower poles were relatively normal.

Operation was performed on the fourth day after admission.

DIFFERENTIAL DIAGNOSIS

DR. GEORGE G. SMITH: The question in this case is whether a twist of the torso sustained while the patient was walking, without any actual fall, could cause bleeding from trauma of a normal kidney.

I do not believe it would. I think it might if the patient had renal stone or hydronephrosis or some pathologic condition in the kidney, which might be ripped or torn by any unusual motion.

The fact that the bleeding occurred during all parts of micturition is rather against a prostatic origin. Usually, blood from the prostate precedes urination—not always, but usually. Furthermore, there was no dribbling, hesitancy or incontinence, and nothing to substantiate a diagnosis of prostatic bleeding.

The answers to two questions would be helpful. Did the patient have any bladder residuum? Was the blood seen coming from the ureter or any particular source at the time of cystoscopy?

DR. TRACY B. MALLORY: Can you answer either of those two questions, Dr. Gens?

DR. JOHN P. GENS: There was no bladder residuum, and no blood could be seen coming from either ureter at the time of cystoscopy.

DR. SMITH: Was the patient bleeding at the time?

DR. GENS: No.

DR. SMITH: It is a good thing to cystoscope patients with hematuria at the time there is blood in the urine, because then one can get an indication of the origin of the blood, which one often cannot get later on.

The fact that cystoscopy failed to reveal the papillary growth probably means that the alleged papilloma was a blood clot adherent to the bladder wall. It is very difficult to distinguish between an adherent blood clot and a papilloma that has been bleeding and is infiltrated with blood. With kidneys that show as good a renal function by non-protein nitrogen and phenolsulfonephthalein tests as this man's kidneys did, one expects to see a very good picture of the kidney pelvis from the Diodrast or Ncoskiodan, whichever one was used, unless he was not well prepared and had a great deal of fluid.

From the story to date, I have not the slightest idea what this man was operated on for. May we see the x-ray films?

DR. LAURENCE L. ROBBINS: These are the films of the intravenous pyelograms, and as noted, there is no good visualization of the calyces, pelvis or ureters. The retrograde pyelogram, in contrast, shows these very obvious bilateral pressure defects in the outlines of both pelvis. They are nearly symmetrical, but there is more involvement of the superior calyx on the left.

DR. SMITH: They are excellent and unusual films, I should say. The simultaneous bilateral occurrence of tumor is possible, but very unusual. It is much more likely that the patient had bilateral solitary cysts. The pelvis and calyces do not give the picture of congenital polycystic kid-

neys. Furthermore, the renal-function tests are too good for a case of polycystic kidneys in a man of this age. On the other hand, there is very definite pressure here, as Dr. Robbins has pointed out. The uppermost calyx is thinned out over a presumably smooth, symmetrical round tumor. It is quite possible to get marked hematuria from solitary cyst of the kidney, perhaps owing to interference with the blood supply, sometimes with rupture of the cyst. I should make a diagnosis of bilateral solitary cysts of the kidneys. I do not know which side I should operate on or why, but that is my diagnosis.

DR. MALLORY: Would you have operated on this patient on this evidence?

DR. SMITH: I suppose he could have had a tumor on one side and a cyst on the other, but it would be unusual to have the findings so symmetrical. If he had had successive episodes of bleeding and if observation had shown that he always bled from one side, I should be inclined to operate on that side. If it were a tumor, I should take out that kidney, and if it were, as seems more probable, a solitary cyst, I believe that removal of such a cyst would check the hemorrhage and that it would be to the patient's advantage to operate.

DR. WILLIAM B. BREED: Without that evidence, where would you operate?

DR. SMITH: As I say, I should want to know from which side the bleeding was coming. We do not know that from the history.

DR. BREED: Well, where are you going to operate—midline, right or left?

DR. SMITH: I should guess that the left kidney would be the one to pick because the upper calyx appears to be more involved in the x-ray film than the one on the other side, but I do not believe that is sufficient reason for selecting that side. I should insist on knowing which side was bleeding, and if this elderly man stopped bleeding and had no symptoms, I should leave him alone.

DR. J. DELLINGER BARNEY: What about bilateral adrenal tumors?

DR. SMITH: These lesions very evidently involved the structure of the kidney itself—the parenchyma of the kidney. So far as I know, adrenal tumors do not do that; they push the kidneys down but do not invade them.

DR. FLETCHER H. COLBY: It would add to the interest of the discussion if Dr. Smith were told the next step.

DR. MALLORY: We are prepared to do that. Dr. Gens, will you proceed?

DR. GENS: We never did know from which side the bleeding was coming. When the patient was admitted to the hospital, the gross hematuria stopped. The urine on both sides showed red blood cells. We decided to operate on the right

side because we believed that the chance of cyst was greater on the left side since the calyces were actually involved on the left side, whereas the tumor was pushing the pelvis or the calyx away on the right side, which would be more like neoplasm. Therefore, we operated on the right, came down on a cyst and treated it in the usual fashion.

DR. MALLORY: Would you then wish to do anything more, Dr. Smith?

DR. SMITH: I should assume that there was a cyst on the other side also, and unless he bled again or had further symptoms, I do not believe I should operate.

CLINICAL DIAGNOSIS

Cortical cysts of kidneys.

DR. SMITH'S DIAGNOSIS

Bilateral solitary cysts of kidneys.

ANATOMICAL DIAGNOSES

Solitary cyst of right kidney.

Papillary adenocarcinoma of left kidney.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Suppose you go ahead with the story, Dr. Gens.

DR. GENS: About seven days later, although the patient had a perfectly uneventful immediate postoperative course, he once more had gross blood in the urine.

DR. SMITH: May I ask what you did to the right kidney?

DR. GENS: We excised the wall of the cyst. Then we decided to aspirate the left side but did not obtain anything but a few drops of blood, although we were fairly certain that we had touched the tumor mass in the left kidney.

DR. SMITH: But you knew the blood was coming from the left side?

DR. GENS: No.

DR. SMITH: I believe I should have looked in the bladder to see if the blood were coming from the left side.

DR. MALLORY: I think by exclusion it was believed that the hemorrhage must have been coming from the other side.

DR. SMITH: I think that is assuming too much; however, it probably was so. But I do not believe one can take anything that is easily demonstrated for granted. One could easily put in a small cystoscope and look at the ureters.

DR. MALLORY: Eventually, the patient was explored on the left side, an obvious tumor was found, and a nephrectomy performed. He made an uneventful convalescence. The tumor proved to be a papillary adenocarcinoma of renal origin.

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THE SPREAD OF INFANTILE PARALYSIS

It is difficult to correlate the fact that the incidence of infections of the upper respiratory tract is lowest and that of poliomyelitis—a disease in which the upper respiratory tract is generally considered to be the important, if not the only, portal of entry of the virus of infantile paralysis—highest during the late summer and early fall. This view concerning the origin of poliomyelitic infection has been based chiefly on the following facts: the virus of poliomyelitis has been demonstrated in nasal washings obtained in the early stages of the infection, the disease, during out-

breaks, is considered to occur with more than the expected frequency in relation to tonsillectomy, and it is relatively easy to infect the susceptible monkey with the virus by intranasal inoculation.

Recent experimental work, however, indicates that the nasal passages may constitute a point of exit as well as of entrance for the virus of poliomyelitis. Thus, the virus has been recovered from the nasal secretions of monkeys infected by inoculation into the brain and even into the peritoneum. Furthermore, in monkeys inoculated intranasally, the virus disappears from the nose a few hours later and reappears there after a lapse of about forty-eight hours.

Increasing evidence is being brought forth to implicate the gastrointestinal tract as the route of infection in poliomyelitis. This, of course, is much more consistent with the seasonal incidence of the infection, and the long known association of epidemics of the disease with the course of rivers and in relation to other bodies of water. Even as early as 1912, Kling and his colleagues,¹ in Sweden, reported the finding of the virus of infantile paralysis in the stools of human cases. This observation has been confirmed and extended sporadically by a number of workers, but intensive investigations based on this finding have been carried out only during the last three or four years.

Briefly, it has now become clear that the virus of poliomyelitis can be demonstrated quite readily in the stools of frank cases and of so-called "abortive cases." In fact, the virus can be found much more frequently and over much longer periods in the stools than in the nasal passages. The specific virus has also been identified in the stools of a large percentage of intimate, but healthy, contacts of cases, as well as in the sewage from homes and areas where the disease is prevalent. Furthermore, it has been shown to exist in the stools of patients and carriers for considerable periods. These findings have recently been reviewed by Armstrong² and by Paul.³

The ease of identifying the virus of poliomyelitis in stools has proved to be of the greatest help in epidemiologic studies of this disease. Re-

cently, Piszczek, Shaughnessy, Zichis and Levinson⁴ reported the results of their studies of an outbreak in a suburban community in Cook County, Illinois. The outbreak involved 15 cases between June 4 and July 11, 1941. In 3 out of 4 patients, the virus of poliomyelitis was demonstrated in samples of feces collected about one month after the onset of symptoms. The virus was also found in the stools of at least 8 out of 48 contacts, but not in the feces of 25 healthy residents of the same community who had had no contact with the disease. In view of previous epidemiologic notions concerning the familial spread of the disease, it is noteworthy that the virus was found in the stools of 2 presumably healthy children who were in contact with adult members of their families who, in turn, became ill with poliomyelitis. The authors succeeded in isolating the virus from a supposedly healthy carrier two months after he had had contact with persons who became ill with poliomyelitis and one month after exposure to his father, who died of poliomyelitis.

The epidemiologic evidence brought to light by these studies seems to point strongly to a spread of the disease by apparently healthy carriers—a view that has been held for over twenty-five years by the Swedish workers, who supported the contention that the infection was spread by way of the gastrointestinal route.

All these findings are beginning to clarify the picture of the epidemiology of infantile paralysis. It is hoped that they will result in the development of effective measures for the control of this disease.

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DRUGS AND MENTAL DISEASE

It is encouraging that drugs and chemical agents are very minor causes of mental disease in Massachusetts: a recent study¹ indicates that of 115,000 patients cared for in Massachusetts mental hospitals between 1917 and 1937, only 841 cases seemed to have been associated with the use of drugs and chemicals. Of these, 36 cases were unverified, so that the actual number was 805 cases, or less than 0.7 per cent. These cases were diagnosed as "psychoses due to drugs and other exogenous toxins," except for cases labeled "without psychosis: drug addiction."

A comparison of these cases with those related to alcoholism originating in the same geographic area during the same period is interesting. According to Dayton,² alcoholism caused more than fifteen times as many entries to state mental hospitals as drugs. Furthermore, many of the patients using drugs also drank alcohol in excessive amounts and therefore might have been classified as alcoholic cases with equal validity: among first admissions related to drugs and chemical agents, 50.4 per cent of men and 25.5 per cent of women were intemperate users of alcohol, and Dayton found that 32.0 per cent of all men admitted with psychoses and 6.0 per cent of all women were intemperate.

It appears that users of drugs are not especially selective in their choice of pharmacologic comforts, since these patients took more than one drug (sometimes three or four) either concurrently or successively.

Many persons in the group stated that their use of drugs began when they were given drugs on prescription by a physician. They may have had the prescription refilled, or the physician may have failed to withdraw the drug when the specific need was over. A few began taking drugs on the advice of friends or relatives, but self-medication was a less important factor than therapeutic use under medical advice. Despite the limited number of cases represented, physicians should be aware of the possibilities that may follow the injudicious use of drugs.

Perhaps the most striking finding in the study, aside from the excessive use of alcohol, was the high incidence of abnormal personality traits and prepsychotic personalities. Many patients had histories of frank mental disease and previous admissions to mental hospitals for reasons unrelated to drugs. It might be assumed that their resort to drugs was a symptom of psychologic illness and that the intoxication or addiction was a result rather than the cause of illness.

The major drugs reported were as follows: opium and its derivatives, 363 cases; barbiturates, 208 cases; and bromides, 101 cases. Many of the cases were suicidal, accidental or due to industrial exposure and cannot be considered in relation to addiction—the standard classification groups cases of this type with all others related to chemical agents.

Among the facts emphasized in this study is the need for the physician to recognize the limitations of medication related to mental disease and to be especially aware that the uncontrolled use of certain drugs may precipitate mental disease in patients who are predisposed, who have histories of previous mental illness or who are inclined to have unstable personality trends. The need for additional investigation into the effect of drugs on personality is evident.

In addition, it is pointed out that the complications of drug addiction may be related to the faulty diets, the avitaminoses and the abnormal regimes of personal hygiene of drug users, as has been shown for alcoholic complications. The heterotropic quality of the addiction pattern in this group is of interest because it seems to demonstrate that one drug can be substituted for another and that, consequently, little additional evidence is needed to demonstrate conclusively that addiction is more basically associated with personality types than with specific chemical agents.

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MEDICAL EPONYM

RAUCHFUSS'S TRIANGLE

Although Carl Rauchfuss (1835-1915) discussed "Die paravertebrale Dämpfung auf der gesunden Brustseite bei Pleuraergüssen (The Paravertebral Dullness on the Healthy Side in Pleural Effusions)" before the Pediatric Society of St. Petersburg in April, 1903, the first published account of his finding appears under the above title in *Verhandlungen der Einundzwanzigsten Versammlung der Gesellschaft für Kinderheilkunde in der Abteilung für Kinderheilkunde der 76. Versammlung der Gesellschaft deutscher Naturforscher und Ärzte in Breslau, 1904* (21:202-211, 1905). A portion of the translation follows:

The clinical finding . . . is the triangular area of dullness, which can always be demonstrated by percussion or palpatory percussion, on the healthy side, along the vertebral column and extending upward to a height that depends on the extent of the pleural effusion, frequently as high as its upper level. The base of the triangle corresponds to the lower border of the lung, and its hypotenuse leaves the base at a distance of 2 to 5 cm. from the spinous processes (in childhood).

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY: POST-PARTUM SHOCK FOLLOWED BY DEATH

A twenty-eight-year-old primipara had had adequate prenatal care. The past history was irrelevant, and at no time during her pregnancy was elevation of the blood pressure or albuminuria noted. There had been no flowing, and the size of the pelvis was adequate. Labor started spontaneously and lasted twenty-six hours until full dilatation. Delivery was difficult because of a transverse arrest, but a living child was obtained. Immediately after delivery, the patient went into shock, the pulse rising to 160 (the blood pressure was not recorded). Extraction of the placenta offered no problem, and there was no unusual bleeding. Eight hours after delivery, the hospital authorities thought the patient to be in such poor shape that they took it on themselves to call an obstetric consultant, who stated that her condition was critical. Although there was no alarming bleeding at this time, she was in profound shock, presenting such typical signs as cold, clammy skin, rapid, weak pulse and low blood pressure. The consultant advised immediate transfusion, but this measure was not carried out at once because the patient's physician saw her soon afterward and

After a year's work in the poorly equipped laboratory, during which he had demonstrated to the profession the wide range of usefulness of the x-ray, Dr. Williams felt the necessity of the services of a professional photographer and mechanic and secured Ernest E. Fewkes, who had done much original work along these lines. The trustees of the Boston City Hospital later appointed Mr. Fewkes to the position of photographer and x-ray assistant to the hospital. That was June 18, 1893, only three years after the discovery of the x-ray. Mr. Fewkes's ability as a photographer, mechanic and all-round scientist enabled Dr. Williams to make great strides in his research work.

Mr. Fewkes received many x-ray burns while working with this light in the days before anything was known of the danger in being exposed to the rays. One by one, he lost three fingers on each hand as the result of burns sustained forty years ago. Later, internal burns developed, which finally resulted in death, which occurred at his home on Hyde Street, Newton Highlands, on July 16.

NOTES

The Massachusetts Society for Mental Hygiene announces the resignation of its medical director, Dr. Henry B. Elkind, effective August 12, when he entered active service as a major in the Medical Corps of the United States Army. Dr. Elkind had served as medical director of the society since 1925, and his able administration brought recognition of the society's leadership in the field of mental-hygiene education, not only in Massachusetts but throughout the Nation. During his directorship, which was characterized by resourcefulness, vision, and energy, he did much to extend the application of mental-hygiene principles to many important fields of community life, including child care, industry, social work, public-school education and teacher training. One particular branch in which he achieved special success is the application of statistics to the study of mental disease, and he is recognized as one of the foremost leaders in the country in the epidemiology of mental disease. Under Dr. Elkind's direction, the Massachusetts Society for Mental Hygiene has adapted its program to meet wartime needs, and he leaves it in a strong position to continue its contribution to the welfare of the community under the changed and difficult conditions of today.

Dr. Frank H. Washburn, of Holden, was recently elected governor of the American College of Chest Physicians at the annual meeting of the college. Dr. Richard H. Overholt, of Brookline, was elected second vice-president.

CORRESPONDENCE

A CORRECTION

To the Editor: It has come to my attention that you have reprinted my article "Unsocialized Medicine," in a special supplement to your journal. I was pleased to have my dissenting remarks included among the newspaper pieces lauding the new prepayment plan of the Massachusetts Medical Society, and was impressed by the profession's tolerance of my somewhat sharp criticisms.

However, you erred in identifying me as "president of the White Cross," and I'd appreciate your correcting this so as not to expose the White Cross (which supported the Massachusetts Medical Society legislation) to professional criticism for my personal views.

Francis H. Russell, now with the State Department in Washington, is president. Edward A. Taft, vice-president

and Boston lawyer, has been acting president during his absence. I functioned only as president of the unofficial but enthusiastic Association of White Cross Members.

HAROLD PUTNAM

The Boston Globe
Boston

* * *

The *Journal* acknowledges its error of referring to Mr. Putnam as president of the White Cross. Incidentally, it is pleased to learn that the views of Mr. Putnam are purely those of an individual and not those of an organization—either the White Cross or the Association of White Cross Members. Ed.

REPORT OF MEETING

BOSTON LYING-IN HOSPITAL JOURNAL CLUB

At a regular meeting of the Boston Lying-in Hospital Journal Club, held at the hospital on April 15, Dr. Edwin H. Place discussed "Contagious Disease in Relation to Obstetrics."

Although this is not a common problem, it becomes important in the individual case so far as care is concerned. There have been only 76 cases of communicable disease during pregnancy or immediately post partum in 50,000 admissions studied at the South Department of the Boston City Hospital. There were 8 deaths, but 4 of these occurred in cases of scarlet fever before the use of sulfonamide compounds, and this is still a serious problem. The task of prevention seems impractical; however, nearly all cases are preventable. It is no longer necessary for the obstetrician to refrain from treating streptococcal cases with the present knowledge of bacteriology and sepsis; but a physician assumes a grave responsibility if he treats these patients when such diseases can be avoided.

If the question arises of admitting for delivery a woman of a family in which scarlet fever has occurred very recently, the finding of a negative Dick test and negative cultures makes her safer than a routine admission. However, routine cultures are impractical because of the lack of knowledge of when or over how long a period prior to confinement they should be carried out. If cultures are contemplated, the staff should be periodically tested, for completeness. The finding of a few streptococcal or diphtheritic carriers in this manner is inconsequential when one considers the many that are missed. If such a program of safety is contemplated, it is better to immunize the carriers so that they will do no harm. On the whole, however, Dr. Place suggests that carriers be ignored, for they cannot be adequately treated and it becomes a burden to isolate them for weeks or months. He believes that pregnant women should be immunized, but most of the urban population is immune anyhow. In diphtheria, the prospective mother alone can be freed of suspicion by culture and Schick test.

If there has been mumps in the home, the woman in urban life will undoubtedly be immune, and if not, the opportunity for spread is remote. There are no good tests in this disease, and one can only rely on these probabilities. The giving of convalescent serum during the incubation period is sound. In chicken pox, the chances that an adult will contract the disease, even if exposed, are small. Measles is of little practical significance, since the children of urban mothers are usually immune.

In general, it has become the accepted policy of large

urban maternity hospitals not to admit any suspicious cases, and such women must be delivered at home under proper precautions or in a hospital for contagious diseases.

The incidence of communicable disease in the newborn is rare, especially those contracted in utero. Measles, smallpox and chicken pox are known to be contracted thus. Only one infant at the South Department of the Boston City Hospital has developed scarlet fever, and the children are always kept with their mothers. On the whole, this disease is rare under one year. Diphtheria is possible but at present unusual.

In discussing some slides, Dr Place made several practical suggestions. Vaccination should never be carried out in the presence of eczema because of the danger of generalized vaccinia. Chicken pox is not contagious when the exanthem is pigmented. When this disease occurs during scarlet fever, all the lesions arrive at once, pass through the stages simultaneously and rapidly, and have the distribution of scarlet fever. The most valuable differentiation of smallpox and chicken pox is the rapidity of the changes in the former in contrast to even slight cases of the latter.

The discussion was opened by Dr Stewart Clifford, who advocated specific admission rules for all outpatient departments. Dr Arthur Hertig presented the case of a four and a half months' fetus with smallpox. He suggested that viruses may cross the placental barrier where as bacteria do not, in general.

In conclusion, Dr Place emphasized the rarity of in utero infections of this type. The question of whether coryza in an adult is actually a minimal whooping-cough infection may be settled by the proper use of cough plates and the finding of lymphocytosis. He believes that the benefit of convalescent serum is overemphasized. There is no center for this in Boston at present. So far as in utero immunity is concerned, it has been proved that the organisms of at least diphtheria, scarlet fever, whooping cough and mumps may pass across the placental barrier and, possibly, may even be concentrated thereby. But urban mothers are invariably immune to these organisms.

He made the following suggestions in answer to Dr Clifford's request for specific outpatient department rules. In diseases in which susceptibility tests are available, these may be carried out prior to confinement when time allows it. In cases of exposure to measles, chicken pox and mumps in the nonimmune mother, convalescent serum is not trustworthy enough to make admission more than a gamble. Such women probably should not be admitted if delivery is expected during the incubation period. If it becomes necessary to admit them, isolation is advised, and not much harm can ensue at worst.

BOOK REVIEWS

Surgery of the Heart By E. S. J. King, M.D., M.S., D.Sc. (Melb.), FRCS (Eng.), FRACS, Major A.A.M.C. 8", cloth, 728 pp., with 4 plates and 268 illustrations. Baltimore: Williams and Wilkins Company, 1941. \$13.50.

This first monograph of any size in the English language on surgery of the heart was written by a thoracic surgeon of Australia. It gives a wide survey of practically all surgical procedures that have been performed, or even

suggested, on the heart and great vessels. In fact, the chief difficulty the reviewer finds with the book is that it is too expansive and includes a good deal of irrelevant matter concerned with medical rather than surgical aspects of heart disease. The volume could profitably be shortened by the omission of much of the material, which can be found in more detail in other books on cardiac physiology and disease.

The work is divided into two sections. The first takes up the anatomy, histology, physiology, embryology and pathology of the heart, with a discussion of roentgenology and electrocardiography. It is this part of the book particularly that might have been omitted or radically shortened to advantage. The second section deals in its introduction with the surgical approach to heart disease and with experimental investigations, and then considers, in order, the various diseases of the myocardium, endocardium, pericardium and great vessels. Of most practical value are the discussions of the treatment of cardiac wounds, foreign bodies and pericardial disease. There is a tendency to overstress surgical relief for myocardial and coronary heart disease, considering their relative unimportance or lack of success. It still remains to be proved how much good can be done for coronary heart disease by any surgical measures, too often, the common tendency for states of coronary insufficiency to correct themselves, no matter what therapy is carried out, is not recognized. There is an inadequate account of the important new operation introduced by Gross and Hubbard, of Boston, for closure of the patent ductus arteriosus.

The book is well arranged, and the frequent historical notes are of especial interest. An ample bibliography is appended to each of the section subdivisions, and should be very helpful for reference. There are numerous illustrations, a few of them in colors; many are helpful in relation to the subject at hand, but a considerable number might usefully have been omitted from a volume with this title. The book is attractively printed and bound.

Nostradamus: The man who saw through time By Lee McCann. 8", cloth, 421 pp. New York: Creative Age Press, Incorporated, 1941. \$2.75.

In the last few months, there has been a revival of interest in Nostradamus, or at any rate in the prophecies of Nostradamus, which relate to certain world events up to 1999. There are those who pretend to discern, in the forecasts of this sixteenth-century astrologer, specific references to the humiliation of France, to Adolf Hitler and even to Pearl Harbor, although the attack had not occurred when this book went to press. Let those who believe take comfort, after these dark hours, the Axis powers are doomed to defeat. But it will not do to relax, merely on these prophetic grounds.

Two thirds of this book is devoted to a fictionalized biography of Nostradamus, and of the last portion to the predictions themselves, with elucidations of the particular modern events to which they refer. They need elucidation, for they are as obscure as the Apocalypse. But perhaps we have not the requisite faith. Miss McCann has, she is a hero-worshiper, at least of Nostradamus, whose life—he was a successful medical practitioner long before his ventures into world prophecy came to absorb all his energies—is painted as if he were one of the great. Some of us would be more inclined to rank him with Cagliostro or Eliza Perkins.

Symptoms in Diagnosis. By Jonathan C. Meakins, M.D., LL.D. 8°, cloth, 323 pp., with 54 illustrations. Boston: Little, Brown and Company, 1941. \$4.00.

The importance of symptoms in diagnosis is well attested by this book, which is not a text of clinical medicine but rather a survey of symptoms as related to various syndromes and pathologic entities. It is written in a fascinating style, and its readability is enhanced by the elimination of all bibliographic references. Only a master of his field, as Dr. Meakins has proved himself to be, can assume this prerogative.

Dr. Meakins writes: "[The study of symptoms—as part of clinical medicine—] . . . needs young minds untrammelled by superstition and preconceived and fixed ideas which are the most deadly of all impediments to the advancement of medical knowledge. But with all this, there is a wonderful hope that through harnessing exact science in the way of sterol and physical chemistry and their sisters, electrophysics and biophysics, the day is not far hence when this tangle will be unsnarled and there will be gleams of light to illuminate the pathway to truth and understanding."

The pleasure of reading this work is akin to that which the bibliophile derives from browsing among books. Students and practitioners will find this volume particularly valuable.

Diseases of the Blood and Atlas of Hematology: With clinical and hematologic descriptions of the blood diseases, including a section on technic and terminology. By Roy R. Kracke, M.D. Second edition, thoroughly revised, reset and enlarged. 4°, cloth, 692 pp., with 54 color plates and 46 other illustrations. Philadelphia: J. B. Lippincott Company, 1941. \$15.00.

That a second edition of Kracke's large and expensive book is forthcoming within a few years indicates its recognition as a standard text. The reviewer must confess, however, to a certain disappointment, which is perhaps based on his own idiosyncrasies regarding hematologic exposition. These derive from two fundamental and related concepts: that the hematologist is no longer a pathologist, but a clinician with a knowledge of the laboratory, and that hematology has advanced a long way from its previous preoccupation with the blood cells as the be-all and end-all of the subject. Hematology is now internal medicine, physiology and physiologic pathology, biochemistry and pathology. For these reasons, a work by a pathologist, however broad his outlook, must have its shortcomings, which indeed this volume possesses. Fully a third of the volume deals with variations in the morphology of the blood cells, with the result that the physiologic pathology and clinical features of some conditions are often not sufficiently stressed. There seems to be much absorption with systematization, terminology and classification, which savors of the ponderous Teutonic texts, formerly so popular. On the other hand, the pictures of blood smears and cells far outrank anything else in this country and for the *Atlas* alone, the book is worth owning. The lithography is unusually good.

There are excellent sections on agranulocytosis, in which the author did some of the pioneer work, and on leukemia. In the description of such preponderantly clinical conditions as pernicious anemia, idiopathic hypochromic anemia and the hemolytic anemias, however, the discussion is often pedantic, immersed in too many quotations from various authors and impeded by too much classification. For example, hemolytic anemia is discussed separately from hemolytic jaundice, although physiologically they are related conditions. The statement that the fragility of the

red cells is always normal in acquired hemolytic anemia does not agree with numerous recent observations. Perhaps because the author is primarily a pathologist, considerations of therapy are often not only scant but misleading. This holds true not only for the treatment of acquired hemolytic jaundice, in which splenectomy is brushed aside as having little or no value, but also in the management of an acute case of idiopathic thrombopenic purpura. The statement is made that "splenectomy should not be attempted in the patient who has the disease in the acute form with severe hemorrhages, nor should it be done in those who are in a bleeding episode even though the course has been chronic." Unfortunately, many a patient has been lost—usually through cerebral hemorrhage—while physicians have been debating and temporizing. It is particularly in the acute form that splenectomy must frequently be done as an emergency measure. With a good surgeon, the risk is slight, and far less than that involved in temporizing.

The descriptions of thrombopenic purpura, polycythemia and Cooley's anemia are scant, and there is only a short paragraph on erythroblastosis foetalis. There is no discussion of the recently much discussed entity of leukoerythroblastic anemia associated with ectopic myeloid metaplasia. However, von Jaksch anemia, which has been regarded as defunct, rates a large paragraph. On the other hand, Custer's section on the bone marrow is good, as is the one on malaria and on hematologic technic.

In general, this is a good one-volume text on hematology, excellent for its histologic descriptions and pictures, but lacking somewhat in physiologic and clinical feeling. The printing and format are excellent, and the index and bibliography are good.

Eye Hazards in Industry: Extent, cause and means of prevention. By Louis Resnick. 8°, cloth, 321 pp., with 33 illustrations, 13 tables and 2 charts. New York: published for the National Society for The Prevention of Blindness by Columbia University Press, 1941. \$3.50.

For the guidance of safety engineers, industrialists, workers and the medical profession in the prevention of eye injuries in industry comes this third volume in the past twenty-five years, published for the National Society for the Prevention of Blindness, and posthumously by the author Louis Resnick, who records his two decades of first-hand contacts with factories, mills and mines in the conservation of vision.

The first portion of the book deals with the problem of ocular hazards in industry, with especial reference to accidents, diseases of the eyes and defective vision. Each year in this country 300,000 workmen suffer eye injuries costing employers and employees the total of \$200,000,000, 98 per cent of which are preventable. The author estimates that 80,000 workmen in this country have lost one eye and that 8000 workmen have lost both eyes as a result of preventable injury.

The second portion of the book deals with the solution of the problem through safety design, mechanical guards and reduced hazard at the machine; through safety devices to shield the eye; through adequate illumination; and through education of the workmen in the proper use of the appliances.

All statements are well supported by statistical evidence, and the book carries four appendices that contain useful information about industrial poisons hazardous to the eyes, minimum standards of illumination, and industrial welfare organizations.

(Notices on page ix)

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ERYTHEMA NODOSUM*

M. H. POPPEL, MD,[†] and A. M. MELAMED, MD[‡]

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DURING the years 1928-1941, 88 patients were discharged from the Mount Sinai Hospital, New York City, with a diagnosis of erythema nodosum. These cases were reviewed from two standpoints to analyze the clinical data from the point of view of associated diseases, and to determine whether any specificity to the mediastinal or hilar adenopathy, or both, is shown roentgenologically.

ETIOLOGY AND INCIDENCE

The etiology of erythema nodosum, a doubtful tuberculide, is not known. Originally, it was believed to be an acute specific febrile and mildly communicable disease. Accumulating evidence (Spink,¹ and Paul and Pohle²) suggests that it is not a specific pathologic entity but a nonspecific toxic complex with many precipitating or provoking factors. It may occur during the course of various conditions, both infectious and non-infectious.

It is three to five times more prevalent in females and most frequent in young persons. It is rare in children under the age of three and in very old people. It is most prevalent during the spring season. The incidence of erythema nodosum, as well as the type of disease it is associated with, varies with the habitat, type and age of the patients, according to other series reported in the literature.

Wallgren³ has shown that in Scandinavian children 95 per cent of the cases of erythema nodosum appear with tuberculosis, in England, this percentage is 70, and in this country it is lower. He believes that in tuberculous children the erythema nodosum appears when the child becomes tuberculin sensitive.

In adults, less emphasis has been placed on

tuberculosis as an etiologic factor and more on rheumatic fever and streptococcal infections (Paul and Pohle²). Keil,⁴ after a critical study of the subject, believes that erythema nodosum is not of rheumatic origin.

Dickson⁵ has called attention to the association of erythema nodosum and coccidioidomycosis as seen in the San Joaquin Valley, where the latter is known as "valley fever" or "desert fever."

PATHOLOGY

Grossly, the lesions of erythema nodosum consist of discrete, firm, hot, tender conical elevated nodules about 1 to 5 cm. in diameter and symmetrically distributed. The lesions appear most frequently over the anterior aspects of the legs and less frequently over the forearms, arms, thighs, buttocks and face. The average case shows about eight to ten nodules, which have a glossy surface and vary from a bright red to a deep purple. As the nodules begin to regress, they undergo the color involutions of a bruise or contusion.

Histologically, these erythematous nodules suggest nonspecific inflammation. Ormsby⁶ describes the changes as "vascular dilatation, marked edema of the collagen, small round-cell infiltration, largely perivascularly arranged in the middle and lower portions of the corium and to a lesser extent in the papillary and subpapillary portions." He also points out that epidermal changes are usually absent.

ANALYSIS OF CASES

This analysis is based on a clinical diagnosis of erythema nodosum made on discharge from the hospital. The patients did not come under our personal clinical observation. In this series of 88 cases, the condition was three times more prevalent in females, and the ages of the patients ranged from two to fifty-eight years (Table 1).

*From the Department of Radiology, Service of Marcy L. Sussman, Mount Sinai Hospital.

[†]Instructor in radiology, New York University College of Medicine and assistant radiologist, Mount Sinai Hospital.

[‡]Formerly resident in radiology, Mount Sinai Hospital.

Associated Diseases

Many diseases and conditions were found to be associated with erythema nodosum. Often, two or more conditions or complaints occurred in the

TABLE 1. *Age and Sex Distribution in 88 Cases of Erythema Nodosum.*

AGE	FEMALE NO. OF CASES	MALE NO. OF CASES	TOTAL
yr.			
1-9	7	7	14
10-19	10	7	17
20-29	22	3	25
30-39	10	2	12
40-49	8	0	8
50-59	9	3	12
Totals	66	22	88

same patient, either preceding or during an attack.

In 13 cases, no evidence of associated disease was present. The remaining 75 cases were found to be associated with the following conditions.

Tuberculosis. Four cases were associated with tuberculosis.

The first patient, a five-year-old boy, entered the hospital on November 17, 1928, with two soft-tissue masses, one in the region of the elbow and the other in the region of the ankle. Tubercle bacilli were recovered from the aspirated contents of the soft-tissue masses. Enlargement of the cervical, axillary, epitrochlear, inguinal and submaxillary lymph nodes was found. There was no pulmonary infiltration or mediastinal or hilar adenopathy in the chest roentgenograms. The patient died fourteen months later as the result of tuberculous meningitis.

The second patient, a six-year-old boy (Case 11, Table 2), had enlargement of the mediastinal and hilar nodes on the first roentgenogram of the chest. Eighteen days later, the chest was re-examined and showed, in addition to the previous findings, widespread nodular pulmonary infiltrations bilaterally. The tuberculin test was strongly positive. Autopsy performed at another hospital eight months later showed hematogenous miliary tuberculosis involving the lungs, meninges and practically all the other viscera. The mediastinal and hilar lymph nodes were involved by caseous tuberculosis.

The third patient (Case 7, Table 2), a nine-year-old boy, showed a pneumonic infiltration extending from the left root to the periphery of the left upper lobe and enlarged hilar nodes. The tuberculin test was strongly positive. Physical examination revealed enlargement of the cervical and epitrochlear lymph nodes. The clinical discharge diagnosis was childhood pulmonary tuberculosis. The patient failed to report for follow-up studies.

The fourth patient (Case 14, Table 2), a thirty-four-year-old woman, had been under observation in the Out Patient Department for the previous ten years. A tuberculin test performed seventeen days after the onset of erythema nodosum yielded a strongly positive local reaction, with generalized symptoms of malaise, fever and so forth. Seventeen days later, or thirty-four days after the appearance of the erythematous nodules, one of the lesions on the right leg ulcerated. Biopsy of one of the lesions on this leg showed the changes of erythema nodosum. A roentgenogram of the chest revealed numerous fibrocalcified areas in both upper lobes. Calcifications in the cervical nodes were also seen on the left side of the neck. There was no evidence of recent pulmonary infiltration or consolidation, and guinea-pig inoculation of the gastric contents revealed no evidence of tuberculosis. Within several months, three additional crops of erythematous nodules appeared. The chest roentgenogram remained the same.

Rheumatic heart disease. Of the 7 patients with definite rheumatic heart disease, 2 developed the erythematous lesions while in the hospital during episodes of cardiac decompensation.

There were 10 additional patients with questionable rheumatic heart disease. In 1, in whom rheumatic nodules developed on the ninth and twenty-first days of hospitalization, there was no evidence of heart disease. In the region of the elbows, the nodules of erythema nodosum and the rheumatic nodules were present simultaneously, but were easily differentiated clinically. When this patient returned for follow-up study two years later, there was still no evidence of heart involvement.

Chest roentgenograms were taken in 6 of the 7 cases associated with definite rheumatic heart disease, and in none of these were there any intrathoracic abnormalities, such as enlarged nodes and pulmonary infiltration.

Upper respiratory infection. Most of the 49 cases in this group were associated with upper respiratory infections of streptococcal origin. This group included cases of so-called "grippe," pharyngitis, tonsillitis, sinusitis, peritonsillar abscess and bronchitis. The majority of these patients entered the hospital with a history of illness lasting from a few days to about two weeks. Half showed evidence of peripheral lymphadenopathy. Chest roentgenograms were made in 34 cases of this group, and in 11 there was evidence of enlarged mediastinal or hilar nodes. Clinically, 5 patients of the latter group also had enlargement of the cervical nodes.

Arthralgias. In erythema nodosum, the complaint of joint pain or arthralgia is difficult to evaluate. One must attempt, and often one is unable, to differentiate a true joint pain from pain that is secondary to the inflammatory changes brought about by the erythematous lesions, particularly when the lesions occur in the vicinity of joints. In this series, 28 patients complained of joint pains. There was no abnormality in the 14 patients whose chests were examined by x-ray.

Ulcerative colitis. Six patients with acute or chronic ulcerative colitis developed lesions of erythema nodosum. The chest was examined roentgenologically in only 1 case, in which no abnormality was shown. Another case of ulcerative co-

received 60 gr. of sulfanilamide before the appearance of the erythema nodosum.

In this group of 8 cases, only one roentgenogram of the chest was available, in which no abnormality was noted.

Syphilis. Four patients presented past histories of syphilis, but in none of these was the blood Wassermann or Kahn test positive. Roentgenographically, 1 case (Case 4, Table 2) showed a resolving left-lower-lobe pneumonia, with moderate enlargement of the bronchial nodes bilaterally. Chest roentgenograms of 2 other patients in this group showed no abnormality.

Gonorrhea. None of the 4 patients with past histories of gonorrhea showed evidence of active

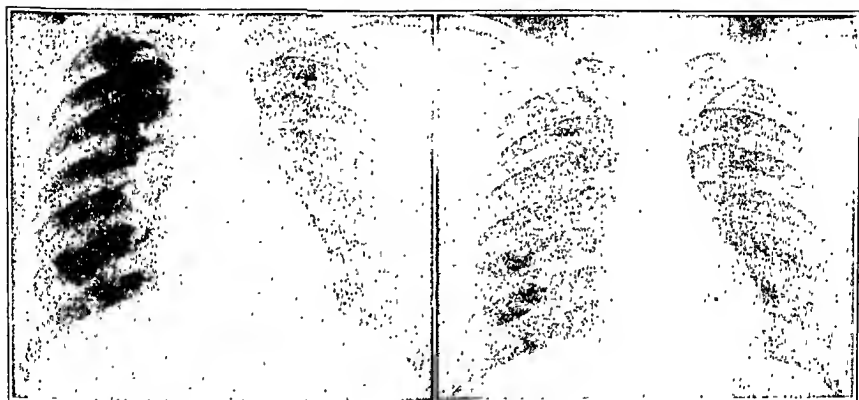


FIGURE 1.

The x-ray film on the left shows enlargement of the mediastinum and hilar lymph nodes in a case of erythema nodosum in which there was no demonstrable associated pulmonary disease; the film on the right was taken four weeks later, when there was essentially no adenopathy.

litis, which was not included in this survey, developed lesions that resembled erythema nodosum, but the diagnosis of acute perivascularitis was not excluded.

Drug ingestion. In only 2 patients of a group of 8 with a history of drug ingestion was there strong evidence that the eruption was due to drug intoxication. In both cases, bromides were found in the urine, and in 1 there was a past history of veronal poisoning. The drugs that were found to be related to or ingested prior to the appearance of erythema nodosum were bromides, coal-tar derivatives, potassium iodide, sulfanilamide, Neoprontosil and sulfathiazole. One patient received therapeutic doses of sulfanilamide for three days before the onset of the eruption. This patient was being treated for a prostatic abscess. Another had

infection except, perhaps, for the patient with a prostatic abscess, alluded to previously, who received sulfanilamide prior to the occurrence of erythema nodosum.

Herpes zoster. One patient developed herpes zoster on the dorsum of a hand in the same region as the lesions of erythema nodosum twenty-six days after the onset of the erythema. The roentgenogram of the chest was normal.

Measles and otitis media. One patient stated that the onset of erythema nodosum was preceded by measles and bilateral otitis media three weeks and two weeks, respectively, before hospitalization. The chest roentgenogram was normal.

Eye diseases. Conjunctivitis was present in 4 cases. One of these patients had ulcerative colitis a year previously. Another developed an epi-

scleritis during the course of the eruption, and also developed iridocyclitis two months following discharge from the hospital. Of this group of 5 patients, chest films were available in 4 cases, none of which showed any abnormality.

Prostatic abscess. This patient, previously referred to in the section dealing with drug ingestion, stated that he had had gonorrhea thirty years before entering the hospital in 1940 with a prostatic abscess. Roentgenologic examination of the chest was not performed on this patient.

Postoperative infection. Erythema nodosum lesions were described in a patient who had developed a wound infection following a surgical procedure for repair of an incisional hernia.

Axillary abscess. One patient, a nurse, developed erythema nodosum during the course of an axillary abscess. An axillary lymph node was removed histologically, and the findings are described below. The chest of this patient was not examined roentgenologically.

Peritonsillar abscess. While being treated for a peritonsillar abscess, one patient developed the lesions of erythema nodosum. Roentgenologic examination of the chest showed no abnormality.

Tuberculin Tests

Of the forty-four tuberculin tests* that were performed on half the patients, thirty-three were positive. No tests were performed subsequent to discharge from the hospital.

Previous Attacks

Five patients entered the hospital with histories of previous episodes of erythema nodosum. Three patients stated that they had had two, four and five previous attacks respectively, whereas 2 claimed that they had had one previous attack each. Another case had a questionable previous attack.

Subsequent Attacks

Two patients of the group returned with attacks of erythema nodosum. The patient with evidence of bilateral fibrocalcific tuberculosis developed three subsequent crops of erythematous lesions within a period of about five months following the initial episode of erythema nodosum.

History of Exposure to Tuberculosis

Three patients presented evidence of contact with tuberculous patients; only 1 of these showed slight enlargement and calcification of the hilar lymph nodes. Five patients entered the hospital with histories suggestive of possible contact with tuberculosis, 3 of whom roentgenologically showed intrathoracic abnormalities.

*O.T. (old tuberculin) is used for these tests; in children and in adults in whom tuberculosis is suspected, the initial dilution is 1:100,000, and in other adults, 1:10,000, a test is not reported "negative" until a 1:1000 dilution has been employed.

Communicability

Two employees of the Mount Sinai Hospital who were roommates developed erythema nodosum lesions five days apart. In both, there was a history of an upper respiratory infection preceding the eruption.

Biopsy

Biopsies were performed in 10 of the 88 cases of erythema nodosum. Specimens were taken from the skin in 8 cases and from lymph nodes in the axilla in 2. The microscopic findings in the skin sections in all cases were those of erythema nodosum. In 1 case with concomitant lymphadenopathy, an axillary lymph node that was removed showed nonspecific hyperplasia. The lymph node removed from a patient with an axillary abscess of a few months' duration showed nodular areas with small central abscesses. Epithelioid cells were seen, but no tubercle bacilli were present.

Subsequent Case Records

Thirty-four patients returned for follow-up examinations. One patient, subsequently showed questionable evidence of rheumatic heart disease, and another returned seven years later with an episode of acute rheumatic fever with joint symptoms. Hypertension was noted in 2 patients who reported for examinations following discharge from the hospital. Two others returned with recurrent episodes of eruptions diagnosed as erythema nodosum.

Roentgenologic Features

Chest roentgenograms were available in 56 of the 88 cases. Fourteen of these were associated with pulmonary changes or enlargement of the intrathoracic lymph nodes, or both.

There was roentgenologic evidence of enlargement of mediastinal or lymph nodes, or both, in 12 patients, 3 of whom showed calcification in the nodes.

The hilar shadows were accentuated in 2 cases, and in another there was unusual exaggeration of the pulmonary markings in both upper lobes.

A resolving pneumonic process was noted in 1 case.

In the presence of a clinical diagnosis of childhood tuberculosis, the roentgenogram showed a pneumonic infiltration of the left upper lobe.

A young patient who later died of hematogenous miliary tuberculosis showed nodular infiltrations throughout both lungs.

A thirty-four-year-old woman whose chest roentgenogram revealed fibrocalcific tuberculosis of both upper lobes on several occasions developed episodes of erythema nodosum. The chest findings remained unchanged.

TABLE 2 Data on Patients with Associated Intrathoracic Changes

CASE No.	HOSPITAL No.	DATE OF ADMISSION	SEX	AGE	CHEST ROENTGENGRAM	TUBERCULIN TEST	COMMENT	SUBSEQUENT COURSE
1	320104	2/20/30	F	40	2/21/30 moderate enlargement of left hilar lymph nodes	Not done	Four previous attacks of erythema nodosum during previous 30 years tonsillitis preceded these attacks	March 1931 no recurrence after removal of tonsillar tissue
2	35070	4/8/33	F	9	4/10/33 slight enlargement of hilar lymph nodes with calcification calcified primary infection left base slight elevation of pericardium on anterior aspect of right tilt beneath soft tissue swelling of erythema nodosum lesion	Positive	Mother of patient receiving pneumothorax therapy for pulmonary tuberculosis	1934 another attack of erythema nodosum chest roentgenogram showed no change
3	359578	11/23/33	F	5	11/23/33 slightly enlarged hilar nodes particularly on left side	Strongly positive	Generalized lymphadenopathy	1938 chest roentgenogram revealed no change systolic murmur persists rheumatic heart disease (?)
4	361770	1/20/34	F	30	1/22/34 moderate enlargement of bronchial lymph nodes bilaterally with slight calcification resolving left lower lobe pneumonia	Positive	Systolic murmur at apex biopsy of skin on two occasions showed changes consistent with diagnosis of erythema nodosum intravenous and intramuscular therapy given 10 years previously following two miscarriages blood Wassermann reaction negative	4/2/34 no complaints
5	364252	3/30/34	F	29	4/4/34 right bronchial and para tracheal lymph nodes enlarged	Not done	Cervical lymph nodes palpable sister died of tuberculosis 25 years previously	Patient failed to report for follow up
6	366529	5/23/34	F	13	5/25/34 calcified lymph nodes at both lung roots prominence of pulmonary conus	Positive	Bilateral submandibular and axillary adenopathy systolic murmur at base (rheumatic heart disease?) electrocardiogram normal	Patient failed to report for follow up
7	375748	1/17/35	M	9	1/19/35 pneumonia infiltration extending from left hilum to periphery of lung in midportion of left upper lobe, enlarged left hilar nodes	Strongly positive	Bilateral cervical and epitrochlear lymphadenopathy clinical diagnosis childhood pulmonary tuberculosis	1/31/35 chest roentgenogram showed moderate decrease of pneumonic infiltration in left upper lobe no subsequent record
8	378461	4/5/35	M	13	4/6/35 unusual exaggeration of pulmonary markings of both upper lobes	Positive	Systolic and presystolic murmur (rheumatic heart disease)	1941 no cardiac murmurs
9	412329	8/3/37	F	25	8/4/37 left hilar lymph nodes enlarged	Positive	Chest roentgenogram of patient's father showed evidence of old and questionable recent tuberculosis	November, 1937 pain in region of left upper lobe with slight fever four weeks previously
10	421390	3/14/38	F	16	3/17/38 lateral roentgenogram showed enlarged tracheobronchial lymph nodes prominent pulmonary conus	Positive	Cervical adenitis systolic murmur at apex, 1933 attack of erythema nodosum	June 1939 occasional asthmalgias heart normal
11	433021	12/3/38	M	6	12/6/38 widening superior mediastinum bilaterally due to enlarged nodes exaggerated pulmonary markings somewhat nodular in character, particularly on right side 12/24/38 widespread nodular infiltrations bilaterally nodes enlarged, 1/11/39 no essential change	Strongly positive	Rachitic chest deformity spleen palpable, clinical diagnosis miliary tuberculosis	Death at Seaview Hospital on August 3, 1939 post mortem findings diffuse hematogenous miliary tuberculosis, lungs showed miliary tuberculosis and the enlarged hilar and mediastinal lymph nodes revealed caseous tuberculosis
12	453063	2/28/40	F	25	3/7/40 hilar shadows accentuated on both sides moderate enlargement of mediastinal and hilar lymph nodes	Negative	Residual strabismus from attack of meningitis at age of 2	2/3/41 almost complete regression of previous chest findings
13	476893	7/28/41	F	32	8/1/41 distinct exaggeration of right hilar shadows and slight widening of superior mediastinum to the right appearance most likely due to enlarged hilar and paratracheal lymph nodes	Strongly positive	Skin biopsy not reported, past history "water on kidney" 10 years previously	November, 1941 patient recently admitted to another hospital with hydropneumothorax and hypertension
14	374634	5/7/41	F	34	5/21/41 fibro-sclerotic foci in both upper lobes no definite recent infiltration	Strongly positive	Skin biopsy showed changes due to erythema nodosum	November 1941 patient subsequently developed new crops of erythema nodosum on three occasions in previous 5 months

Table 2 presents a more detailed analysis of the 14 patients with intrathoracic changes.

In view of these findings, it is obvious that roentgenologic examination of the chest should be performed in all cases of erythema nodosum, even in the absence of chest complaints. Examination of the chest in the lateral position should be included. In our experience, in the 1 case in which a roentgenogram in this position was available, an enlarged lymph node was demonstrated, although the routine posteroanterior film failed to reveal it. It is probable that had the chests been examined in both positions routinely, more cases with enlarged intrathoracic nodes might have been discovered. In questionable cases of enlargement of the intrathoracic lymph nodes, more information may be secured by fluoroscopy and sectional radiography, and perhaps also by kymography.

SUMMARY AND CONCLUSIONS

A survey of 88 cases of erythema nodosum indicates that the condition may be found during the course of various diseases, both infectious and noninfectious, virus, bacterial, chemical and toxic. It is evident that no common agent causes these diseases that might be expected to be the cause of erythema nodosum. In a small group of patients (approximately 15 per cent), no evident associated disease was present.

The following conditions were associated with the erythema nodosum in these 88 cases: tuberculosis (4 cases); rheumatic heart disease (7 definite and 10 questionable cases); ulcerative colitis (6 cases); upper respiratory infections (49 cases); arthralgias (28 cases); drug ingestion (8 cases); inactive syphilis (4 cases); gonorrhea (4 cases); herpes zoster (1 case); measles and otitis media

(1 case); eye disease (1 case); prostatic abscess (1 case); postoperative infection of abdominal wall (1 case); axillary abscess (1 case); and peritonsillar abscess (1 case).

Fourteen of fifty-five available chest roentgenograms revealed positive intrathoracic findings. Twelve showed slight to moderate enlargement of the nodes, three with calcification. Pulmonary abnormalities were noted in 5 cases—resolving pneumonic process, pneumonic infiltration, exaggerated pulmonic markings, miliary tuberculosis and fibrocalcific tuberculosis. Tuberculin tests, which were performed in 12 of the 14 patients, were positive in 11.

The patients whose roentgenograms showed intrathoracic adenopathy or pulmonary infiltration, or both, had associated disease of the respiratory tract that could account for the abnormalities and often obviously did. In the cases in which the development of erythema nodosum was associated with ulcerative colitis, prostatic abscess, peritonsillar abscess, rheumatic heart disease, gonorrhea, conjunctivitis, postoperative infection, axillary abscess, measles and otitis media, and ingestion of drugs, the chest roentgenograms failed to demonstrate any pulmonary changes or intrathoracic lymphadenopathy.

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A PRACTICAL OUTLINE FOR THE TREATMENT OF BURNS*

DONALD W. MACCOLLUM, M.D.†

BOSTON

FOR several years before the present war, the number of people in this country who died each year from burns ranged in the vicinity of 6000. In addition, 1500 died each year as a result of conflagration, and untold thousands lived but were permanently disfigured or deformed. Since burns are not acquired or inherited like disease, but are almost always purely accidental, more and more rigid safety measures have been instituted both in the home and in industry in an attempt to reduce these figures. Obviously, if fewer people were burned, there would be fewer deaths, but prevention is only one of the two significant factors concerned in this high death rate. The other, equally important, factor is a proper appreciation of how to handle the burned patient from a medical standpoint. To lessen the incidence of confused, unintelligent and inadequate care by the layman, nurse and physician alike would effect an appreciable reduction in the number of fatalities and deformities caused by burns.

During peacetime, 83 per cent of all burns occur in the home, 10 per cent in industry, and 7 per cent in public accidents. It is obvious from these figures that there is a great need for both an educational program and the elimination of physical hazards in every home. This is to be kept in mind now and after the war is over. However, in wartime, with the possibility that explosive and incendiary bombs will drop on civilian rather than on military lines of defense, the number of burn casualties is in danger of being greatly increased. This has been true in every country that has experienced any number of air raids. For this reason, every person should have some knowledge of what to do and, perhaps more vital, what *not* to do for a person who has been burned.

The Red Cross and the Office of Civilian Defense have accepted and are discharging a tremendous responsibility in training a large number of laymen in the rudiments of first aid. Every physician in the country has also been preparing and refreshing his mind, so that he will be equipped to take care of war casualties.

In line with this general preparation, the follow-

ing condensed outline for the treatment of burns has been drawn up, based on experience both personal and collective, to aid in the rapid assimilation of the present knowledge on this subject.

I. THERMAL BURNS (HOT LIQUIDS, STEAM, FLAME, AND HOT METALS)

1. First-Aid Instructions for Laymen.

a. Treat all burned patients for shock.

b. If a physician is not present but is available:

(1) Cover small burns with a clean cloth or sterile bandage, and take the patient to the first-aid post.

(2) For extensive burns, cover the patient with a clean sheet and blankets; bring the doctor to the patient, if possible—otherwise send the victim to a hospital immediately.

(3) Do *not* put tannic acid ointment on any burn.

c. If a physician is neither present nor available and it seems likely that one or two hours may elapse before the patient can be seen by a physician:

(1) For small burns, clean the area by gently washing with a mild soap under running water—if running water is not available, do not clean, but cover the burn with a paste of sodium bicarbonate and water; wrap the burned area securely in clean or sterile cloths, and send the patient to a physician.

(2) For extensive burns, remove the clothing but do not try to clean the area; cover the burned parts with clean cloths (napkins, pillow cases or sheets) soaked in a warm solution of sodium bicarbonate—cover with dry cloths; keep the patient warm and get him to a hospital as soon as possible; give strong coffee or tea by mouth.

d. Important points to be remembered:

(1) Do *not* apply tannic acid jelly or strong tea to a burn until after the burn has been properly cleaned by a doctor.

(2) Do *not* apply grease in any form.

(3) Do *not* move the patient about in an attempt to put on a neat bandage; disturb him as little as possible.

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†From the Department of Surgery, Harvard Medical School, and the Surgical Service of the Children's Hospital and of the Peter Bent Brigham Hospital.

†Associate in surgery, Harvard Medical School; associate visiting surgeon, Children's Hospital; associate in plastic surgery, Peter Bent Brigham Hospital.

2. First-Aid Instruction for Physicians.

a. Check all patients with minor or major burns for shock; treat this even before the burned area is examined.

b. Give morphine liberally: administer a dose double that which would normally be used for the patient if he were to have a preoperative dose for an elective operation.

c. If shock is severe, administer oxygen by mask or tube and give caffeine intramuscularly; if plasma is available, give 5 cc. per pound of estimated body weight intravenously; if plasma is not available, give physiologic saline solution—10 cc. per pound of body weight—while plasma is being obtained.

d. When shock has been effectively combated, carefully remove the bandages and clothes; examine the burn and try to estimate extent and depth of the burn.

e. If the burn is minor:

(1) Cleanse thoroughly by washing gently for about seven minutes with sponges soaked in 50 per cent green soap (solution, not tincture) and 50 per cent hydrogen peroxide.

(2) Break all blisters, and remove all dead skin and debris (use sterile instruments).

(3) Flush with copious amounts of physiologic saline solution, or distilled water, and dab dry.

(4) Dust the area with sulfathiazole, sulfadiazine or sulfanilamide powder.

(5) For burns of the hands, feet, face and genitalia, apply a sterile ointment and cover as well as possible with sterile gauze and bandage.

(6) For burns elsewhere on the body tannic acid jelly or triple-dye jelly may be used; cover with sterile gauze, apply an Ace bandage, and splint the part involved.

f. If the burn is major:

(1) Remove the clothes sticking to the burn and gross dirt or contamination, but do *not* clean *extensively*.

(2) Dust the area liberally with sulfathiazole, sulfadiazine or sulfanilamide powder (if a 5 per cent sulfadiazine, water-soluble jelly or emulsion is available, this may be used instead of the powder).

(3) If the powders are used, cover the area with a liberal amount of water-soluble glycerin-tragacanth jelly (if this jelly is not available, any sterile ointment or triple-dye

jelly can be used; however, the latter are harder to remove when the burn receives its final débridement).

(4) Apply heavy (5 to 7 cm. thick) sterile gauze pads and hold them securely in place under mild pressure with an elastic bandage.

(5) Evacuate the patient to a hospital as quickly as possible.

g. Important points to be emphasized:

(1) Do *not* fail to appreciate the fact that shock must be treated *first* and that examination of the burn should wait until the patient is fairly well recovered from the shock.

(2) Do *not* apply tannic acid in any form until *after* the burn has been *thoroughly* cleansed; never apply it to the hands, face, feet or genitalia.

(3) Do *not* temporize with morphine—give it either in a large enough dose to do some good or not at all.

(4) Do *not* allow the sulfonamide powders to get into the eyes or up the nose (they irritate as foreign bodies).

(5) Do *not* fail to apply a *thick* dressing under mild pressure.

3. Hospital treatment of fresh burns.

a. For minor burns treat the patient as outlined above (Section I, 2e, 1-6).

b. For major burns:

(1) Check on the degree of shock still present; administer more morphine, heat and so forth, as required.

(2) If time permits and facilities are available, obtain a red-cell count, hemoglobin determination, hematocrit reading and a serum protein (one or more of these are helpful in determining the degree of hemoconcentration).

(3) Give an initial intravenous infusion of plasma of 3 to 5 cc. per pound of estimated body weight; have more plasma available if it is needed; whole-blood transfusion is not indicated unless there has been appreciable blood loss from some other source; if whole blood is available but no plasma, make an effort to separate the plasma from the red cells by centrifugalization or otherwise.

(4) After shock is well controlled, the patient may need to be anesthetized for proper cleaning; use rectal or intravenous anesthetics for those who may have inhaled hot air or gases.

(5) Wash burned area thoroughly for seven minutes with a mixture of solution of green soap and hydrogen peroxide (equal parts)

(6) Remove all dead skin and debris, use sterile precautions throughout debridement

(7) Flush thoroughly with physiologic saline solution and, if desired, some mild antiseptic, such as a 1:1000 solution of Zephiran or Merthiolate, or ST 37

(8) For burns of the hands, feet, face and genitalia, dust the area with one of the sulfonamide powders and cover with a sterile ointment (*tulle gras*) and a heavy layer of gauze sponges held in place by an elastic bandage, splint the hands and feet

(9) For burns elsewhere on the body, the treatment outlined in Section I, 3b, 8, may be used, provided adequate facilities are at hand to combat fluid loss by repeated plasma transfusions

(10) For burns elsewhere on the body, the escharotics are usually employed, principally 5 per cent tannic acid followed by 10 per cent silver nitrate, the triple dyes or a sulfadiazine spray, whichever method is used, specialized aftercare is required: a clean or sterile electrically heated bed, frequent evaluation of the blood chemical findings, adequate fluid intake enterally and parenterally, and constant nursing and medical appreciation of the problems for each case

4 Hospital Treatment of Old Burns

a If a sulfonamide powder has been used in the first aid treatment, a débridement as outlined in Section I, 3b, 4-7, may be carried out as late as thirty hours after the burn was received

b If a sulfonamide has not been used, a complete operative débridement is contraindicated if the burn is eight or more hours old. In this event, the following procedure is advised

(1) Give shock treatment as outlined in Section I, 3b, 1-3

(2) Immerse the patient in a tub of warm tap water for one or two hours, with constant inflow and outflow of water

(3) Remove the patient from tub, dab dry and spray with one of the sulfonamide powders

(4) Either cover the burns with an ointment (preferably *tulle gras*) or use the triple

dye jelly or sulfadiazine spray, do not use tannic acid in any form

(5) As an alternative to the procedure outlined immediately above, one may use dressings wet with physiologic saline solution, a Bunyan envelope or *tulle gras* with Eusol (125 gm chlorinated lime, 125 gm boric acid and 1000 cc distilled water—let the mixture stand twenty four hours, then filter and keep in a tightly corked bottle), if the burn is coated heavily with fibrin and pus, one of the latter is preferable first, to be followed later by a sulfonamide powder

c In second degree burns, healing takes place without grafting over a period of ten days to two weeks

d In either superficial or deep third degree burns (so called "third degree," "fourth degree" and "fifth degree," according to one system of classification), grafting may be necessary, depending on the extent and site involved

e If grafting is necessary, certain precautions must be observed before proceeding

(1) The patient must be free from infection, in good health and with a normal red cell count

(2) An estimate of the amount of tissue to be replaced must be made, and a program outlined for its transfer

(3) The granulations must be flat, firm and cherry pink

(4) The granulations should be removed down to the fibrous tissue base from which they spring, and depending on the site involved, this fibrous base may also be removed

(5) For defects involving the loss of skin only, a thin or thick razor graft (Thiersch or split Thiersch) is preferable

(6) For small areas involving the skin of the face or hands, a full thickness graft (Wolfe or Wolfe-Krause) may be used interchangeably with the thick razor graft

(7) For areas involving the loss of both the skin and subcutaneous tissue, a single hinged or double hinged pedicle flap (pedicle, gruntlet, tube or rope) must be used

(8) Bone, cartilage and fascia may also be replaced, but this is usually done six to eight months after the skin defects have healed

(9) Do not use island grafts (pinch, Reverdin, small deep and Davis grafts) unless

nothing else is possible; there is seldom occasion for their use.

II. CHEMICAL BURNS

(Whoever treats chemical burns should take adequate precautions to protect himself.)

1. Mustard Gas.

a. First aid for exposure to mustard-gas vapor (one to eight hours).

(1) Remove and place all clothes in decontamination bucket.

(2) Give a thorough soap-and-water bath, including shaving or clipping short of all hair and rewashing these areas.

(3) Apply a bleaching-powder wash, followed by a second soap-and-water cleansing.

(4) Keep the patient under observation for twelve hours; if there is no rash or blisters at the end of that time, the patient may be discharged.

b. Late treatment for exposure to mustard-gas vapor (eight hours and over):

(1) Treat the patient for shock; rash and blisters have appeared over warmed areas of the body (axilla, groin and so forth), with severe itching and beginning shock.

(2) Do *not* sedate heavily with morphine (pulmonary complications due to inhalation of the gas may be increased by a lowered respiratory rate).

(3) Anesthetize by the rectal or intravenous route, if necessary.

(4) Clean the burn thoroughly, as outlined in Section I, 3b, 5-7.

(5) Apply *tulle gras* over all raw surfaces and follow with a heavy dressing wet with equal parts of Eusol and mineral oil.

(6) Apply a heavy dressing, held in place with gauze and an Ace bandage under mild pressure.

(7) Follow the routine outlined for the aftercare of second-degree or third-degree thermal burns (Section I, 4e, 1-9).

(8) For very late infected cases seen two or three days after exposure, follow the routine outlined in Section I, 4b, 1-3, 5.

c. First aid for contact with mustard-gas liquid.

(1) Within five minutes, *blot* off excess mustard gas by dabbing with dry pads.

(2) Dab the area gently and repeatedly with pads moistened in kerosene, gasoline or alcohol; wring the pads out so that excess liquid will not drip on the patient and spread the burn.

(3) Thoroughly wash the entire area with a mixture containing equal parts of green soap and peroxide.

(4) Wash the area again with alcohol.

(5) Dry by blotting, and apply a dry dressing that is to be removed and the area examined every two hours for the next twelve hours; if the area looks normal at the end of twelve hours, the patient may be discharged.

d. Late treatment for contact with mustard-gas liquid.

(1) If blisters have formed, dab with pads of kerosene gently to get rid of excess liquid; do *not* use a bleaching agent.

(2) There is no need to sedate heavily or anesthetize (the area is usually painless after liquid has penetrated through the skin).

(3) Carry out full débridement as outlined in Section I, 3b, 5-7, and follow with a *tulle gras* and Eusol dressing.

(4) In very late cases when the blisters have broken and have become infected, carry out the routine outlined in Section I, 4b, 2, 3, 5.

(5) In the late cases, as soon as the fibrinous infected coat has been removed from the raw surfaces by the Eusol, the sulfonamides may be used.

(6) Late care, including grafting, is the same as that for thermal burns.

2. Lewisite.

a. First aid for exposure to lewisite vapor.

(1) Remove clothing at once.

(2) Wash entire body with hydrogen peroxide; follow this with a complete and thorough bath with soap and water and an alcohol sponging.

(3) Keep the patient under observation for 12 hours; if no blisters appear, he may be discharged.

b. Late treatment for exposure to lewisite vapor.

(1) Sedate and give a rectal or intravenous anesthetic if burns are extensive.

(2) Wash around and over each blister with soap and hydrogen peroxide; be very gentle.

(3) Break the blister, being very careful to catch all the blister fluid on a sponge (throw sponge in decontamination bucket); immediately apply a pad wet with hydrogen peroxide to the raw area; renew this pad frequently.

(4) After all blisters have been broken and covered with a pad of hydrogen peroxide, carry out full operative débridement as outlined in Section I, 3b, 5-7.

(5) Cover the burn with a *tulle gras* and Eusol dressing, thick gauze and an Ace bandage.

(6) If the burn remains clean, reapply the dressing described in Section II, 2b, 5, each day.

(7) If the burn becomes infected, the treatment is the same as that outlined in Section I, 4b, 2, 3, 5.

c. First aid for exposure to lewisite liquid

(1) Within one minute after exposure remove the clothes and start treatment.

(2) Swab area with hydrogen peroxide repeatedly for thirty minutes.

(3) Wash with soap and water for seven minutes, and follow with an alcohol pad, which is left in place for five minutes.

(4) Pat dry, and apply a dry dressing, if no blisters have formed at the end of twelve hours, the patient may be discharged, if blisters have formed, carry out the routine outlined in Section II, 2b, 2-4, except that anesthesia is usually not necessary.

d. Late treatment for exposure to lewisite liquid

(1) If an unbroken blister is found, carry out the routine outlined in Section II, 2b, 1-7.

(2) If the blister has broken and the patient shows signs of arsenical poisoning, excise entire area under anesthesia at once, and follow by grafting as outlined in Section I, 4e, 5-8.

(3) If the area is too extensive for excision and is grossly infected, the prognosis is poor, however, treat the patient as outlined in Section I, 4b, 2, 3, 5 and attempt to control the arsenical poisoning by intravenous sodium thiosulfate.

3 Phosphorus

a. If there is no phosphorus that is still burning in or on the skin, treat the burn as a thermal one (Section I).

b. If bits of phosphorus that are still smouldering lie on or in the skin:

(1) Wet the area and keep it wet with anything, but preferably warm water (this melts and stops further burning of the

particles; if the area becomes dry, the particles will begin to burn again).

(2) If a 5 to 15 per cent solution of copper sulfate is available, apply this at once (burning is stopped temporarily).

(3) No matter which of the above methods is used, squeeze or pick out the phosphorous particles with forceps and then treat as any thermal burn.

4 Acids and Alkalies

a. Remove the patient's clothing at once, taking care that the chemical agent does not burn others.

b. Flush area under cold running water (the heat of dilution of strong chemicals is carried away by the continuous washing); if running water is not available, douse the patient in a tank, tub, or lake, if the burn is due to lime, brush off the excess before wetting.

c. Do not attempt to neutralize the burning agent (the heat of reaction may cause a deeper burn, or the neutralizing agent itself may burn).

d. After removal of the burning agent, treat as a thermal burn (Section I).

III ELECTRICAL BURNS

I General Effects.

a. Do *not* touch a patient who is still in contact with the electric current, unless proper insulation is possible.

b. Never regard a recently shocked person as dead, even if the heart beat cannot be heard.

c. Continue artificial respiration, oxygen and cardiac stimulants until rigor mortis sets in (several patients have recovered after having been apparently dead for hours).

2 Local Effects.

a. Except for a very few cases almost all electrical burns are of third degree, owing to the intense heat and the coagulation of blood in the vessels supplying the area involved.

b. Do *not* be misled by the apparently innocuous appearance of the fresh electrical burn, institute treatment at once:

(1) Sedation or anesthesia is rarely necessary.

(2) Clean the area thoroughly with a mixture of green soap and hydrogen peroxide and flush with saline.

(3) Apply a sterile ointment, gauze and an elastic bandage; splint the part involved.

(4) Do *not* apply any substance that will form an eschar.

(5) Apply daily dressings under strict aseptic precautions so that the amount of late necrosis and slough may be observed.

(6) Do *not* cut away sloughing tissue; allow the demarcation and detachment of dead tissue to take place without surgical aid (hasty operative removal may result in excision of tissue that will be viable and necessary for repair).

(7) Vessel walls are damaged, so that secondary hemorrhage is frequent; have a

sterile tray with hemostats and a tourniquet always at the bedside.

(8) After the slough has disappeared, treat as in Section I, 4e, 5-8.

A general survey of the treatment of burns has been outlined, with particular emphasis on the treatment of shock, the need for gentleness in the handling of tissues and the necessity for a complete cleansing of the burned area before medicaments are applied. Each burn presents an individual problem; consequently, it is impossible to outline specific details for every possible type of burn. The broad general principles have been stressed, in addition to specific instructions that, if followed within reason, will cause an appreciable reduction in the number of fatalities.

300 Longwood Avenue

MEBARAL IN THE TREATMENT OF EPILEPSY*

BENJAMIN COHEN, M.D.,† AND ABRAHAM MYERSON, M.D.‡

BOSTON AND NORTH GRAFTON, MASSACHUSETTS

IN 1929, the drug known in this country as Mebaral was introduced in Europe under the name of Prominal, the chemical formula being *n*-methylethyl-phenyl barbituric acid. It has been utilized in Europe quite extensively, but its introduction in the United States is recent, so that it is not sufficiently known to the medical profession in this country. Mebaral is supplied in tablets of 0.03 gm. ($\frac{1}{2}$ gr.) and 0.2 gm. (3 gr.) on the erroneous supposition that it is half as potent in sedative qualities as phenobarbital, to which it is closely related chemically. In general, it may be stated that its sedative effect is about one third that of phenobarbital.

In 1932, Weese¹ pointed out that the spans between the hypnotic, narcotic and lethal doses of Mebaral are greater than those of phenobarbital, that is, the margin of safety is greater. In the same year, Blum² reported that he had tried Mebaral for three years on several hundred epileptic patients in his hospital and private practice. He found that 0.2 gm. (3 gr.) two or three times a day decreased the epileptic seizures about 50 per cent. He found it valuable in petit mal as well, and observed no hypnotic effects. Heyde³ considered Mebaral slightly superior to phenobarbital as an anticonvulsant, but greatly superior in the treatment of psychic symptoms in epilepsy.

He favored it for the treatment of ambulatory and noninstitutional patients.

Plaut,⁴ in 1935, stated that the drug was very useful as a sedative, his material being 60 patients suffering from insomnia, nocturnal enuresis, hyperthyroidism and various psychoses. Using it in dosages of 0.1 to 0.2 gm. ($\frac{1}{2}$ to 3 gr.) a day, he found no serious by-effects and noted that employed patients were not incapacitated by drowsiness.

Page,⁵ in 1936, compared his findings with Mebaral and phenobarbital during equal five-month periods. In the period under phenobarbital administration, the patients had a total of four hundred and seventy-six grand-mal seizures. In the second period, under the influence of Mebaral, the same patients had two hundred and forty-four grand-mal attacks. Page also noted that under Mebaral the patients were bright and cheerful, and could care for themselves.

Henderson,⁶ in 1937, selected 13 patients with grand-mal epilepsy who had not shown sufficient improvement on clinical trial with other drugs, and, during a period of twelve months' administration with Mebaral, noted a two-thirds reduction in the number of attacks as compared with those in the previous period. He found that 0.6 gm. (9 gr.) a day was apt to cause drowsiness, and believed that the optimum clinical effects were obtained with 0.4 gm. (6 gr.) a day. His patients did not suffer from gastrointestinal disturbances, urinary changes, or significant fluctuations in blood pressure, and they did not develop a tolerance that required increased dosage. In a few

*From the Division of Psychiatric Research, Boston State Hospital, and the Grafton State Hospital, North Grafton, Massachusetts.

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†Formerly, senior physician, Grafton State Hospital.

‡Professor emeritus of neurology, Tufts College Medical School; clinical professor of psychiatry, Harvard Medical School; director of research, Boston State Hospital.

cases of petit-mal epilepsy, he was not able to produce favorable changes.

Millman⁷, in the same year, reviewed the comparative findings in 39 patients previously on phenobarbital whose medication had been changed to Mebaral with a gradual increase in dosage 50 per cent greater than that of phenobarbital. There was a great reduction in both grand-mal and petit-mal attacks, the average reduction being slightly less than two thirds. Of 27 patients who showed abnormal behavior and were considered to be epileptic equivalents, or psychic manifestations, there was improvement in 19. Many of the adults were given 0.6 gm. (9 gr.) a day for two years, without ill effects. In children, he employed the formula, age—age + 12, to determine the fraction of the adult dose that they should receive. In a few adults receiving maximum dosage, he noted drowsiness, which disappeared when the drug was withheld for a few days.

Our own experience with this drug is threefold. Concerning its value in agitated, depressed and anxiety states, about which we shall report at a later date, it suffices to say that this drug seems to us to be by far the best sedative in the treatment of these conditions, since it produces more tranquility and less narcosis than any other drug, and without untoward symptoms unless given in doses above 0.4 to 0.6 gm. (6 to 9 gr.) a day. Secondly, since the treatment of epileptics in private and outpatient practice is not methodically controlled, it cannot be analyzed well. The impression of both of us is that this drug is efficacious in the treatment of epilepsy, of both the grand mal and the petit-mal types, and that it has fewer undesired effects than either phenobarbital or Dilantin, its chief rivals in the treatment of epilepsy. The third group consists of controlled epileptic patients at the Grafton State Hospital, with which this paper is mainly concerned.

The last group has been known to us for years and represents a group relatively refractory to other drugs. The rate of convulsive expectation had been established over periods of six months to three years of observation. These patients had had previous treatment in this hospital with phenobarbital alone, and with phenobarbital and Dilantin; we here record the experimental treatment with Dilantin and Mebaral, and with Mebaral alone. The comparison is made between the effects of the former two drugs and those of Mebaral on the incidence of epileptic attacks in these patients as compared with the effects of previous drugs used. We are thus not comparing the effects of Mebaral on cases easily controlled by phenobarbital or Dilantin, or by phenobarbital

and Dilantin, but on patients who had not done well on these drugs.

The results of our investigations in these relatively refractory patients may be stated as follows. Of 12 patients who had trial treatment separately with phenobarbital and with Mebaral, 2 did better with the former, and 10 with the latter. On Mebaral alone, there were 42 per cent fewer seizures than with phenobarbital. Nine patients had separate trials of phenobarbital and Dilantin and of Mebaral alone. Two did better with the former, and 7 with the latter. On Mebaral alone, there were 48 per cent fewer seizures than with phenobarbital and Dilantin. Eleven patients had separate trials with a combination of Dilantin and Mebaral and with Mebaral alone. Four did better on the latter, and 7 on the former. There were 38 per cent fewer seizures on Mebaral alone.

The average period for any treatment ranged from twenty seven weeks to one year. We con-

TABLE 1 Comparative Effects of Desultory Preliminary Medication and Concentrated Individualized Therapy with Phenobarbital, Phenobarbital and Dilantin, Dilantin and Mebaral, and Mebaral

PATIENT	AVERAGE NUMBER OF SEIZURES PER TEN WEEKS				
	INADEQUATE PHENO BARBITAL THERAPY	ADEQUATE PHENO BARBITAL THERAPY (56 WEEKS AVERAGE)	PHENOBARBITAL AND DILANTIN THERAPY (23 WEEKS AVERAGE)	DILANTIN AND MEBARAL THERAPY (25 WEEKS AVERAGE)	MEBARAL THERAPY (52 WEEKS AVERAGE)
R. M. Q.	53	—	—	5	5
E. C.	27	6	5	1	2
U. P.	11	4	5	2	3
M. M. C.	13	2	—	1	1
C. R.	14	5	—	3	4
N. S.	8	7	6	—	1
M. W.	23	14	16	13	3
N. H.	6	5	10	9	4
M. H.	6	8	5	4	4
C. C.	19	3	3	3	3
F. H.	18	8	8	16	11
M. H.	11	—	9	12	4
W. L.	9	2	1	—	1

sidered these periods sufficient for determining the value of any drug or set of drugs in patients having frequent attacks.

The dosage of phenobarbital given alone was from 0.13 to 0.45 gm. (2 to 7 gr.) per day, the average being 0.27 gm. (4 gr.). When phenobarbital was combined with Dilantin Sodium, the dosage of the former remained unchanged, and 0.2 to 0.4 gm. (3 to 6 gr.) of the latter was added, the average dose of this drug being 0.3 gm. (4½ gr.). When Dilantin and Mebaral* were used, the daily dose of the former ranged from 0.2 to 0.3 gm. (3 to 4½ gr.) a day, the average being 0.25 gm. (3½ gr.) and that of the latter averaged about 0.6 gm. (9 gr.). When Mebaral was used alone, the dose was from 0.4 to 0.8 gm. (6 to 12 gr.) a day, the average being 0.6 gm. (9 gr.).

*Kindly supplied by the Department of Medical Research, Winthrop Chemical Company New York City

In Table 1, the column labeled "inadequate phenobarbital therapy" indicates the former incidence of seizures during each ten weeks for periods ranging from six to twenty-four months immediately preceding the institution of the program of intensive individualized therapy, which has been described in a previous paper.⁸ That phenobarbital cannot be discredited is evidenced by the fact that this drug alone in adequate amounts reduced the number of seizures 66 per cent from that obtained by desultory treatment.

In a few patients, Mebaral produced drowsiness and gait disturbance, similar to the effects of phenobarbital, although they were less marked and more easily dissipated. We found that amphetamine (Benzedrine) sulfate, in doses of 10 to 20 mg. by mouth, was equally useful in such cases as a therapeutic agent pending the improvement that invariably attended reduction of dosage of Mebaral and rest in bed. In general, such toxic symptoms attended the use of Mebaral much less frequently than the use of phenobarbital, despite the use of proportionately higher dosage.

SUMMARY AND CONCLUSIONS

Attention is called to the value of Mebaral (n-methylethyl-phenyl barbituric acid) in the treatment of epilepsy.

The drug is particularly useful for epileptic children, who prefer tasteless medication, for psychotic epileptics who must be treated by medication concealed in their food, for patients who

cannot be given adequate phenobarbital because of toxic drowsiness and, finally, for trial in patients who do not show satisfactory response after trials of phenobarbital, Dilantin and bromides, separately or in combination.

In certain cases relatively refractory to other medication, significant improvement was noted when Mebaral was utilized.

Mebaral was found to be less productive of toxic symptoms than phenobarbital or Dilantin, and proportionately higher dosage was continued with safety and as great or greater clinical effectiveness.

In the private practice of one of us (A.M.), Mebaral has become the drug of first choice for the treatment and control of grand mal and petit mal. In cases in which it does not work well by itself, it combines very well with Dilantin. In those cases in which it is not effective, it is discarded, and phenobarbital and Dilantin in combination are used.

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HYPOCHROMIC ANEMIA WITH KOILONYCHIA (SPOON NAILS)*

Report of a Case

B. G. CLARKE, M.D.†

BOSTON

KOILONYCHIA (spoon nails), an interesting abnormality, is particularly noted in chronic hypochromic anemia. In the case reported below, koilonychia appeared twice during recurring episodes of hypochromic anemia, disappearing each time after successful treatment of the anemia with iron. Hypochromic anemia is due to iron deficiency, which is essentially dependent on chronic blood loss. Women require about four times as much iron until the menopause as men do, so that hypochromic anemia and, consequently, koilonychia are relatively commoner in women.

*From the Thorndike Memorial Laboratory and the Second and Fourth (Harvard) Medical Services, Boston City Hospital.

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†House officer, Massachusetts General Hospital; formerly, clinical clerk, Second and Fourth (Harvard) Medical Services, Boston City Hospital.

CASE REPORT

First admission. A 46-year-old widowed painter and decorator, who had come to the United States from Glasgow at the age of 22, was admitted to the hospital on January 5, 1934, because of gradually increasing shortness of breath, palpitation and mild ankle edema. Three weeks before admission, he noted substernal tightness on exertion. There was no history of weight loss or melena.

Examination showed a middle-aged man with pallor of the skin, a beefy red tongue, slight pitting edema of the ankles and spooning of the nails. The heart was enlarged, and the blood pressure was 110/60.

Examination of the blood showed a red-cell count of 2,300,000 with a hemoglobin of 20 per cent, and a white-cell count of 6000 with 70 per cent polymorphonuclears, 20 per cent lymphocytes and 10 per cent mononuclears. Red cells in the smear showed marked hypochromia, microcytosis and variation in size and shape. There was only a rare

immature cell, and the platelets appeared normal in number. Gastric analysis showed no free acid, fasting or after histamine. The total acidity was 12 units. Six stools were guaiac negative. The nonprotein nitrogen was 31 mg per 100 cc.

The patient was given iron and ammonium citrates 90 gr a day. The reticulocytes reached 67 per cent on the 7th day, and the red-cell count rose to 4,000,000 and the hemoglobin to 72 per cent 5 weeks later, when he was discharged.

Following discharge, the patient was well and continued to work as a painter for 6 years, without symptoms suggesting either anemia or lead poisoning. He took iron pills intermittently. He continued to be extremely careful about the handling of lead paint and since he is an intelligent man, it is likely that his exposure to this toxic substance was minimal for a painter,

neoplasm or polyp. X-ray examinations of the colon and upper gastrointestinal tract were entirely negative. The reflexes were physiologic, and vibration and position sense normal.

On admission, the red-cell count was 2,860,000 with a hemoglobin of 22 per cent and a hematocrit of 19 per cent, the mean corpuscular volume was 65 cubic microns, the mean cell hemoglobin concentration 24 per cent, and the mean corpuscular hemoglobin 16 micromicrograms, indicating severe hypochromic anemia. The white cell count was 4100, with 72 per cent polymorphonuclears, 19 per cent lymphocytes, 8 per cent monocytes and 1 per cent eosinophils. The red cells showed hypochromia and variation in size and shape. 0.4 per cent reticulocytes were present on admission, and platelets were reduced in the smear. At no time were any stipple cells suggestive of lead poisoning seen. Gastric analysis showed a free acid of 0, a total acid of 4 units and after histamine, a free



FIGURE 1 Nails of the Patient before Treatment

although he had followed this trade since the age of 15. About a year following discharge, the spooning of the nails disappeared.

Second admission (February 20, 1941) The patient had remained essentially well until 6 months before entry, when there was an insidious onset of easy fatigue, weakness, shortness of breath and increasing pallor with development again of spooning of the nails. He had very slight ankle edema, but no tingling or numbness of the extremities, soreness of the tongue, gastrointestinal complaints or weight loss. The diet had apparently been adequate. For the preceding 5 or 6 years however the patient had noticed very occasional streaking of the stools with bright red blood.

Examination showed a well-developed and well-nourished but very pale man in no distress. The skin had a slightly yellow tint, but the scleras were clear. The tongue was pale, with slight atrophy along the margins. The heart was slightly enlarged on x-ray and physical examination with a harsh systolic murmur at the apex and base. The blood pressure was 115/60. The spleen was palpable at the left costal margin, but the liver was not felt. There was no edema of the extremities. Spooning of the fingernails was marked (Fig 1), with cracked margins but no longitudinal striations. Rectal examination revealed skin tags at the anus and moderate sized internal hemorrhoids with several bleeding points. Proctoscopy on three occasions showed no rectal ulcers

acid of 5 units, and a total acid of 10 units. Sixteen stools were guaiac negative, one showed a bloodstreaked exterior and was guaiac positive. The icteric index was 4. Liver function studies including hippuric acid excretion and urobilinogen determinations, were normal. The total protein was 6.3 gm and the nonprotein nitrogen 27 mg per 100 cc.

The patient was given ferrous sulfate, 16 gr a day, supplemented with dilute hydrochloric acid and a high vitamin, high calorie diet. While in the hospital, he was entirely asymptomatic, and showed progressive increase in strength and loss of pallor.

The highest reticulocyte count was 2.8 per cent, but the red cell count and hemoglobin showed a rapid and steady rise until 5 weeks after admission, when the red-cell count was 5,250,000, the hemoglobin 91 per cent, the hematocrit 43 per cent, the mean corpuscular volume 84 cubic microns, the mean corpuscular hemoglobin concentration 27 per cent and the mean corpuscular hemoglobin 22 micromicrograms. After the 1st week the white-cell count rose to levels between 6100 and 13,700. Gastric analysis 4 weeks after admission showed free acid of 8 units and total acid of 56 units, after histamine, the free acid was 18 and the total acid 60 units.

The patient was transferred to the Surgical Service, where three internal and external hemorrhoids were excised, and discharged 6 weeks after admission.

The patient returned to work, taking iron for several

months following discharge. Eight months after discharge, he was entirely well, and the nails had returned to their normal convex contours (Fig. 2). Examination of the blood showed a red-cell count of 5,260,000 with a hemoglobin of 99 per cent, a hematocrit of 46 per cent, a mean corpuscular volume of 88 cubic microns, a mean corpuscular hemoglobin concentration of 33 per cent and a mean corpuscular hemoglobin of 29 micromicrograms, and a white-cell count of 6800.

Comment. The patient gradually developed severe hypochromic anemia coincidentally with koilonychia. On adequate doses of iron, the anemia and koilonychia disappeared, and while taking iron only intermittently, he continued to be well until 6 years later, when anemia and koilonychia again began to develop. Again, these were

first edition of his monograph on diseases of the nails (1900), recorded several additional cases and his original case of a "twenty-five year old, rather chlorotic servant girl," and assigned the name "koilonychia" to the deformity. I have been able to find reports of 83 cases in the literature, in addition to the one reported above.

Idiopathic hypochromic anemia became recognized as a distinct entity after Faber,⁴ in 1913, called attention to the occurrence of a severe type of chlorosis in middle-aged women with gastric acidity. Many subsequent observers have noted

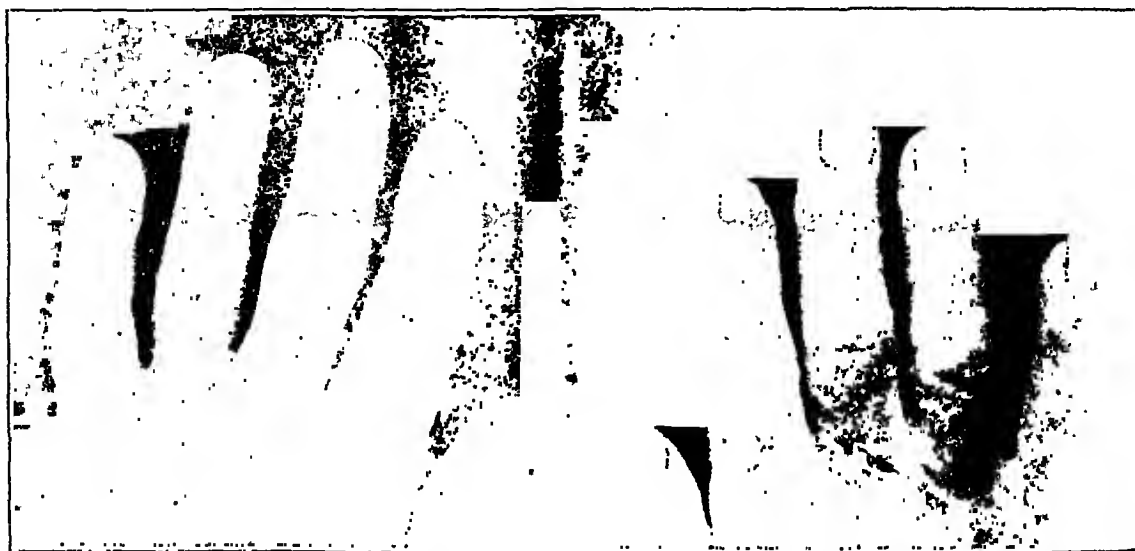


FIGURE 2. Nails of the Patient Fourteen Months after Treatment Had Been Started.

cured by treatment with iron. Hemorrhoids, thought to be the source of chronic blood loss and thus of the iron deficiency, were removed after the second episode of anemia.

DISCUSSION

Koilonychia (*κοῖλος*, hollow; *ὄνυξ*, nail) is characterized by an everted distal edge, flat lateral margins, and a spoonlike central concavity of the fingernail. Any number of fingers may be affected and in varying degrees. Associated changes commonly observed are exaggerated longitudinal striations and increased thinness and brittleness of the nails. These changes are also often found in cases of hypochromic anemia lacking typical koilonychia. Flat nails, a less marked phase of koilonychia, have been specially designated "platonychia" by some writers. A case with similar changes in the toenails has been observed by Eddowes (cited by Crocker¹).

The condition was first described by Ball² in 1874, who presented a case to the Society of Biology at Paris, but did not give it a name. Crocker¹ reported another case in 1896, and suggested the name "spoon nails." Heller,³ in the

koilonychia as a frequent but inconstant feature of the disease.

Idiopathic hypochromic anemia (simple achlorhydric anemia, simple achylic anemia, primary hypochromic anemia, achylic chloranemia, chronic chlorosis, chronic microcytic anemia or essential hypochromic anemia) occurs especially but not exclusively in middle-aged women, and is characterized by an insidious onset, long duration, symptoms common to all severe anemias—including paresthesias, but without objective neurologic findings—and, in addition, glossitis and stomatitis. Splenomegaly, koilonychia, cheilitis (fissures at the corners of the mouth) and dysphagia are often present. In the great majority of cases, there is evidence of disturbed gastric secretion (achlorhydria). The anemia is characterized by ready response to adequate iron therapy, and by a tendency to relapse when treatment is discontinued. Careful study often reveals chronic blood loss without adequate iron intake as a cause of the iron deficiency on which the anemia is based. Iron-deficiency anemia has been reviewed by Wintrobe and Beebe,⁵ Heath and Patek⁶ and others.

There are twelve reports,^{1,7-10} including the present one, comprising a group of 180 cases of idiopathic hypochromic anemia, in which the incidence of koilonychia is stated; it was present in 27 of these cases. In addition, eight observers,^{6,17-23} reporting a total of 365 cases of idiopathic hypochromic anemia, have noted koilonychia in some of the cases under their observation, but have not specified the number in which it occurred.

Flattening, brittleness and exaggerated longitudinal ridging of the nails may be regarded as important signs in cases of idiopathic hypochromic anemia lacking typical koilonychia. Wintrobe and Beebe⁶ found marked longitudinal ridging or, less often, koilonychia, in 40 per cent of their 25 cases, and McGeorge¹⁰ found brittle, thin and flexible nails in half of his 23 cases as well as koilonychia in 1. Davies,⁸ in a study of 55 cases of hypochromic anemia, found koilonychia in 4, 1 of them a postgastrectomy case, and noted flattening of the nails in 21 and excessive brittleness and tenderness in 31.

Most observers^{7-11,21-25} have remarked that in cases under their observation in which the anemia was successfully treated with iron, the nail changes disappeared. Walderström and Hallen²⁵ have reported 3 cases of koilonychia without associated anemia, in 2 of which the nails became normal after iron treatment.

The Plummer-Vinson syndrome of anemia, glossitis and dysphagia can probably be regarded as a group of cases having the clinical and hematologic features of idiopathic hypochromic anemia, with dysphagia as a particularly prominent symptom. A large number of cases have been reported, in 27 of which the observers^{12,24-27} made note of the presence or absence of nail changes. Eight of the 27 patients had frank koilonychia. Ahlborn,²⁸ reviewing 250 cases of carcinoma of the upper gastrointestinal tract, noted frequent appearance of hypochromic anemia, often accompanied by koilonychia.

Faber and his associates²⁰ studied 10 infants, seven to twenty-four months of age, with iron deficiency anemia, none of whom showed koilonychia or glossitis.

A considerable number of other cases of koilonychia have been reported,³⁰⁻⁴⁵ most of them prior to the widespread recognition of idiopathic hypochromic anemia; in a large number of these cases, it was impossible to find a definite causative factor. Several reports,^{2,30-34} however, suggest strongly that exposure of the hands to chemicals may induce or intensify the condition, whereas other observers^{1,33-36} have noted a family history of koilonychia, and in a few cases,^{3,11,37-41}

koilonychia was apparently present from early childhood.

SUMMARY

A case of idiopathic hypochromic anemia with koilonychia recurring at a seven-year interval in a middle-aged man is reported. On each occasion, both the anemia and spoon nails disappeared completely on treatment with iron.

A survey of the literature reveals that koilonychia is not uncommonly associated with hypochromic anemia of the iron-deficiency type, and that less marked nail changes, such as flattening, increased thinness or brittleness and exaggerated longitudinal ridging, are common enough to be of diagnostic help in the disease.

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MEDICAL PROGRESS

VIRUS PNEUMONIAS. I. PNEUMONIAS ASSOCIATED WITH KNOWN NONBACTERIAL AGENTS: INFLUENZA, PSITTACOSIS AND Q FEVER*

MAXWELL FINLAND, M.D.,† AND JOHN H. DINGLE, M.D.‡

BOSTON

SINCE the introduction of specific antipneumococcal serums, considerable interest has been centered on the etiologic classification of the pneumonias. Before sulfapyridine came into use, however, bacteriologic procedures were employed primarily for the purpose of determining the presence of a pneumococcus and its type, with a view to possible specific serotherapy and perhaps also as an aid in prognosis. The recent sulfonamide drugs that have been widely used—sulfapyridine, sulfathiazole and sulfadiazine—are more or less equally effective against all types of pneumococci. These drugs vary to some extent in their effect on other bacteria, such as streptococci, staphylococci and Friedländer's bacillus, which may be involved in the causation of pneumonia. The determination of the causative organism thus becomes as important as the pneumococcus typing.

The increased use of bacteriologic diagnostic methods in pneumonia and, particularly, the widespread employment of sulfanilamide derivatives have brought into relief a group of cases in which the common respiratory pathogenic organisms do not seem to play a role and on which the sulfonamides do not have the usual favorable effect. Some of these cases have a number of distinctive clinical features, and are thought to be of virus etiology. Moreover, pneumonias are known to occur in certain diseases of nonbacterial etiology—that is, in diseases caused by known filterable viruses or by rickettsias.

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*From the Thorndike Memorial Laboratory, Second and Fourth (Harvard) Medical Services, Boston City Hospital, and the Department of Medicine and the Department of Bacteriology and Immunology, Harvard Medical School.

†Assistant professor of medicine, Harvard Medical School; associate physician, Thorndike Memorial Laboratory, and chief, Fourth (Harvard) Medical Service, Boston City Hospital.

‡Associate in medicine and instructor in bacteriology and immunology, Harvard Medical School; assistant physician, Thorndike Memorial Laboratory, Boston City Hospital.

This report deals with the various pneumonias considered to be of nonbacterial etiology, and is divided into two parts. In the first, we present a review of the recent studies dealing with nonbacterial pneumonias associated with known virus or rickettsial agents; these include, chiefly, influenza, psittacosis and Q fever. The second part, which will appear in the next issue of the *Journal*, contains a description of atypical pneumonias of unknown etiology, and a review of the attempts to identify a causative agent in such cases.

INFLUENZA AND PNEUMONIA

The occurrence of serious pulmonary complications in cases of epidemic influenza is well known. Such complications are usually considered to be responsible for the high mortality in certain outbreaks of this disease. Whether the pulmonary lesions are caused by the same agent that gives rise to the influenza itself or are the result of secondary invasions with certain pathogenic bacteria was the subject of considerable controversy during the great pandemics of 1890 and 1918. Most workers considered the influenza bacillus of Pfeiffer to be the significant etiologic agent of both the influenza and its complications during the large epidemic of 1889-1890 and in the smaller outbreaks that followed it.¹ The streptococcus, however, was thought by some investigators, notably Finkler,² to be the cause of the severe and fatal influenzal pneumonias of that period.

Similarly, during the 1918 pandemic, although the influenza bacillus of Pfeiffer was found to be the predominant organism in the lungs in fatal cases of influenza in some regions,³⁻⁷ it was conspicuously infrequent in others.^{8,9} In many localities, the hemolytic streptococcus was apparently the predominant pathogenic organism found during this outbreak, and this organism was particularly frequent in the severe and fatal pneu-

monias complicating the influenza that occurred in many of the camps of the United States Army.¹⁰⁻¹⁴ During the same pandemic, there were a few reports of outbreaks in widely separated areas of a characteristic type of pneumonia complicating the influenza in which *Staphylococcus aureus* apparently played the predominant role.¹⁵⁻¹⁷ Occasional similar cases have been noted in other small outbreaks.¹⁸⁻²²

Very similar pathologic lesions were described by a number of different observers during 1918 and were considered, in a general way, to be the characteristic pulmonary lesions of influenza. In some of these cases, the predominant organism recovered from the lungs was the influenza bacillus^{3, 6, 10} in others the hemolytic streptococcus^{11, 23} and in still others the pneumococcus.^{9, 24} Goodpasture²⁵ observed typical histologic lesions in the lungs of 2 patients in this epidemic, but was unable to demonstrate any pathogenic bacteria in the lungs, by cultural methods, in histologic sections or after animal inoculations. Interestingly enough, neither of these 2 cases was of the acute fulminating variety: one patient died on the seventh day, and the other died during an exacerbation of symptoms that had apparently persisted for more than six weeks after the onset of the original influenza.

It is now generally accepted that some filterable virus, identical with or closely related to that originally demonstrated by Smith, Andrewes and Laidlaw²⁶ and later found by Francis,²⁷ was probably the causative agent in most of the widespread epidemics of typical influenza that have occurred in the last few years. This virus has been labeled "influenza A virus."²⁸ Viruses immunologically identical with or very closely related to influenza A virus have been shown by direct isolations or by serologic tests to be the causative agent in the extensive epidemic of 1936-1937^{29, 31} and also in the one that occurred in 1940-1941.²⁹⁻³⁵ In smaller and more localized outbreaks, another virus, now called "influenza B virus," was found to be the cause,³⁰⁻³² and there is indirect evidence that possibly a third one and perhaps still others give rise to the characteristic clinical picture in some limited outbreaks.^{33, 30}

These findings, however, have not entirely clarified the question of the etiology of the pneumonias that accompany the influenzas during outbreaks. There is some evidence^{20, 21} that even cases of simple and apparently uncomplicated influenza may have a spread of the infection to the lungs. The commonest lesion resulting from such an extension, according to Stuart-Harris and his co-workers,²¹ who reported on the 1936-1937 epidemic in England, is a diffuse bronchiolitis,

which may be distinguished by characteristic physical signs and x-ray shadows. They believe that this represents essentially a true virus lesion because of the relative frequency with which virus was isolated from such cases.

Scadding,²⁰ in a study made during the same epidemic, distinguished a group of cases of typical influenza with abnormal physical signs in the lungs, with or without radiologic evidence of consolidation. In the less severe cases of this group, only areas of suppressed breath sounds were made out at the lung bases. In some of the severer cases, the clinical picture was that of edematous lung bases without abnormal x-ray findings, whereas in others there were definite areas of consolidation, both clinically and roentgenographically; only the latter cases were associated with a high mortality. The bacteriologic flora of the sputum in this group was very similar to that of cases without influenza, except that pneumococci were apparently more frequent in the cases with consolidation.

Both Stuart-Harris et al.²¹ and Scadding²⁰ described cases of fulminating pneumonia in which the influenza A virus and *Staph. aureus* were isolated from the same lungs at autopsy; the authors believed that the cases were almost certainly due to both these agents. Stokes and Wolman,²² in 1940, reported a similar case in which both influenza A virus and *Staph. aureus* were isolated from the lungs. In the 1940-1941 epidemic, a number of cases of severe *Staph. aureus* pneumonia complicating clinical influenza were reported from several clinics,⁴¹⁻⁴³ and the relation of the influenza A virus to some of them was presumptively established.^{41, 42} At the Boston City Hospital, *Staph. aureus* was found in almost pure culture or as the predominant organism in all types of cases of influenza, varying from the mild and apparently uncomplicated ones to the fulminating acute and fatal cases with pneumonia, and including a number with a severe and protracted course.⁴⁴ Evidence of infection with influenza A virus was obtained in all the various types of cases,³³ either by isolation of the virus or by serologic tests. Interestingly enough, sulfathiazole and sulfadiazine seemed to have a beneficial effect in most of the cases but not in the very fulminating ones. These drugs, however, may have been responsible for the recoveries in some of the very serious cases.

All these findings indicate that under certain circumstances the influenza virus itself may set up a considerable bronchopulmonary reaction, but that in most cases in human beings secondary infection with bacteria plays an important role and

may alter the pathologic picture in the lungs. Analogies are to be found in different animal species.⁴⁵⁻⁴⁹ In the ferret and in the mouse, for example, the virus alone may produce pulmonary lesions almost identical with those found in fatal cases in human beings, and no pathogenic bacteria can be cultivated from the lungs in these animals.⁴⁶⁻⁴⁸ In swine, on the other hand, an influenza virus—either the swine strain or a human A strain—gives rise to a mild infection limited to the upper respiratory tract, and pulmonary lesions in this animal result only from the simultaneous infection with the virus and the swine influenza bacillus.⁴⁹ In the human disease, it appears that both the virulence of the influenza virus and the prevalence and virulence of the co-existing pathogenic bacteria determine the occurrence and severity of the complicating pneumonias.

Furthermore, pneumonias may appear in patients with influenza during the height of the original attack, or they may have their onset after a varying interval, following apparent recovery from the influenza. In the latter event, it may not be possible to obtain the virus when the patient is first seen during the attack of pneumonia, but serologic tests at that time may reveal a high antibody titer characteristic of patients convalescent from the virus infection.^{33, 50, 51} These are evidently relapses of bacterial infection developing in patients recovering from influenza. Typical pneumococcal lobar pneumonia, hemolytic streptococcal or pneumococcal bronchitis or tracheitis and even simple tonsillitis occur under such circumstances.²¹ Francis⁵¹ recovered influenza virus on the second day in a patient with pneumococcus Type 3 pneumonia, and Pearson et al.³³ demonstrated high titers or significant rises in titer of influenza A antibodies in many cases of typical pneumococcal lobar pneumonia occurring during the 1940-1941 epidemic in Boston. Such findings indicate that influenza and other severe pulmonary infections may occur simultaneously, or that such infections may follow shortly after an attack of influenza.

PSITTACOSIS, ORNITHOSIS AND RELATED DISEASES

A human disease, resembling influenza on the one hand and typhoid fever on the other and associated primarily with atypical pulmonary lesions and acquired from sick parrots, has been known since 1880.⁵² Numerous small sporadic outbreaks of such infections, always attributable directly or indirectly to exposure to sick exotic birds, mostly of the psittacine family, were described during the following fifty years. In the years 1929 and 1930, however, there was a pandemic of the dis-

ease, having its origin in an epizootic among imported Brazilian parrots but first reported in human cases in Buenos Aires. It was only after this outbreak had spread through many countries all over the world that the disease, psittacosis, gained considerable prominence. It was during this pandemic that the clinical, epidemiologic and pathological aspects of the disease were clearly recognized and its virus etiology was definitely established. A comprehensive review of the early history of the disease and of the outbreak in England is given in the report of Sturdee and Scott,⁵³ which contains an excellent clinical description of the human disease by Levy-Simpson. This report also contains the classic studies of Bedson and Western, which, together with those of Krumwiede and Armstrong and their associates^{54, 55} in this country, established the filterable-virus etiology of the disease. The virus was found to be associated consistently with minute coccobacillary bodies that are now commonly known as "L.C.L. bodies" after Levinthal,⁵⁶ Coles⁵⁷ and Lillie,⁵⁸ the three workers who described them almost simultaneously in Germany, England and the United States, respectively. These bodies are now generally considered to be the elementary bodies of the virus. Enders⁵⁹ has recently reviewed the various aspects of the disease and the present status of our knowledge concerning the virus that causes it in a symposium on virus and rickettsial diseases at the Harvard School of Public Health. Meyer,⁶⁰ in a recent DeLamar Lecture, presented a comprehensive summary of the biology of the virus and its occurrence in human and avian infections.

There are several reasons for the present intensive interest in psittacosis. First may be mentioned the similarity of this disease to the atypical pneumonias that are now being encountered. In reading the details of the earlier proved cases of psittacosis and the clinical descriptions of that disease that have since been given, one cannot help being impressed with the striking resemblance to the current cases so far as the symptoms, physical signs, roentgenologic and pathological findings and course are concerned. The outstanding differences in the prevalent pneumonias are the failure to obtain a history of exposure to birds, except in certain rare cases that are referred to below; the failure to identify the virus of psittacosis by the usual means^{61, 62}; and the lower mortality. In relation to the mortality, one must consider the lower age incidence of the recently reported cases. Most of the deaths from psittacosis have occurred in persons over forty years of age, and the prevalent pneumonias are uncommon in that age group. Furthermore, secondary pneumonias due to bacterial agents have been men-

tioned in cases of psittacosis, but they have not been encountered in the atypical pneumonias now prevalent.⁶³ This may have accounted for some of the fatalities from psittacosis.

A second reason for the awakened interest in psittacosis is the demonstration of many striking similarities and close antigenic relations between the agent of that disease and a number of other recently discovered viruses.⁶⁴⁻⁷⁰ Some of these new viruses—those of lymphogranuloma venereum, trachoma and inclusion conjunctivitis—have no constant or apparent relation to acute pulmonary infections. Others were isolated from laboratory animals inoculated with materials obtained from patients with atypical pneumonia or with influenzalike infections. Still others, which were discovered as apparently normal inhabitants of the respiratory tract of certain laboratory animals, are capable of inducing pulmonary lesions in those animals under specified experimental conditions.

Interestingly enough, some of these viruses, such as those of lymphogranuloma venereum, trachoma, inclusion blennorrhea and mouse pneumonitis,⁶⁹ are susceptible to chemotherapy with the common sulfonamides, whereas others, including the agents of psittacosis and meningopneumonitis, are apparently not affected.⁷¹ The findings in experimental infections seem to correlate to some extent with published results of sulfonamide therapy in the corresponding clinical conditions. Although sweeping conclusions cannot be drawn from the data thus far available, further investigations of this group of viruses not only may be of theoretical interest but also may uncover new information of value in practical therapy.

Finally, recent studies have indicated a widespread occurrence of psittacosis or psittacosishlike viruses in increasing varieties of species of birds all over the world. They have been demonstrated in birds living in the wild state⁷²⁻⁷⁴ and in those bred in aviaries,⁶⁰ and have recently been found in pigeons⁷⁵⁻⁸³ and in barnyard fowl.^{82, 83} Evidence for latent infections under these conditions has come either from demonstration of the virus in the tissues or by serologic tests in large numbers of birds. These latent infections may, under suitable conditions, become activated and give rise to spontaneous infections or epizootics among birds, or they may give rise to cases in human beings.⁷⁹⁻⁸¹ Many of the details of these findings have been summarized by Meyer,⁶⁰ who has suggested that the general term "ornithosis" be used to describe the infections in birds or human infections contracted from birds. The designation "psittacosis" would then be reserved for the psittacine infection. The characteristic pulmonary infection might appropriately be called

"ornithotic pneumonia" or "pneumonia ornithosa."

A few of the recently uncovered facts about psittacosis that are of immediate interest may be mentioned briefly. Widespread latent infection has been demonstrated among the common varieties of pigeons and doves, even among those found in the parks of New York City.^{80, 81} Epizootics have been described in many pigeon lofts, and cases in human beings have been traced to this source. The latent infection in pigeons may be activated by dietary deficiency.⁷⁵ Meyer,^{82, 83} also reported an epizootic among barnyard fowl in New Jersey. This outbreak, which was associated with human infection, may have originated from a sick dove, which roosted among the chickens shortly before they manifested evidences of infection.

It is remotely possible that certain aspects of this problem may have some significance for armed forces based in far-off lands. Such widely scattered countries as Iceland,⁷⁴ South Africa⁷⁰ and Australia^{72, 73, 84} have figured in the recent reports concerning psittacosis. Viruses very similar to that of psittacosis have been isolated from young fulmars, which are birds of the petrel family living on the cliffs off the Faroe Islands and off Iceland, and they were also found in materials obtained from human patients who had acquired their infection while trapping these young birds for eating purposes.⁷⁴ In several parts of Australia, epizootics have been described in various species of parrots living in the wild state, and dead birds infected with psittacosis have been found in the bush.^{72, 73} Under normal circumstances, the infection of wild birds is usually latent, and is transmitted with difficulty to human beings. From what is already known, however, it is not difficult to imagine situations in which serious human epidemics might arise.

Other Viruses

Other viruses may affect the respiratory tract, although their main clinical manifestations are due to involvement of other systems. In general, the symptoms are those of a grippelike or influenzalike infection. Involvement of the lung to a degree sufficient to give signs by physical or x-ray examinations is rare. The virus of lymphocytic choriomeningitis is an example of such an agent.^{85, 86} In experimental animals, vaccine virus may produce a pneumonia whose pathology is similar to that of the atypical bronchopneumonias in man.^{87, 88}

Rickettsial Infections

The virus of psittacosis and the related viruses are rather large and pass only the coarser bac-

terial filters. They have many morphologic and other characteristics of rickettsias, but no arthropod vectors have been established. Rashes do not occur regularly in psittacosis. These agents have therefore not been classified as rickettsias, although Lillie⁵⁸ had suggested that the psittacosis virus be included among them. They may be said to represent a sort of transitional group between the true filterable viruses and the rickettsias.^{66, 67}

Pulmonary lesions, however, have been recognized as part of the clinical and pathological picture of severe rickettsial diseases, notably in typhus and in Rocky Mountain spotted fever.^{59, 90} In typhus fever, physical signs of extensive pulmonary consolidation are sometimes made out on routine examination of patients who run the usual course, but the appearance of such signs is usually accompanied by an aggravation of the disease and a fatal outcome.⁹⁰ At least in some cases, these pulmonary lesions probably represent infection with the rickettsia and not secondary bacterial infection. Pulmonary complications have recently been reported in cases of South African tick-bite fever,^{91, 92} another of the known rickettsial diseases. Experimentally, characteristic lesions have been produced in the lungs of laboratory animals with several varieties of rickettsias, including the different types of typhus, *fièvre boutonneuse* and Rocky Mountain spotted fever.^{93, 96}

Q FEVER

Like psittacosis, Q fever is of considerable interest at present. The agent of this new disease is quite prevalent in certain parts of Australia and has been isolated and identified in some of the western states in this country. Definite evidence of infection with the agent has been found in this country in certain cases with clinical features closely resembling those of the current atypical bronchopneumonias. The relevant facts about Q fever and its causative agent are therefore briefly reviewed.

Australian Q Fever

In 1937, Derrick⁹⁷ described a new pathologic entity occurring in the state of Queensland, Australia, and gave it the name of "Q fever." Cases, which were first noted early in 1933, increased in frequency in August, 1935. A total of 20 cases had been recognized among 800 employees of one abattoir at the time of the original report, and 9 of the cases were described. Other cases not in meat workers were also noted. Blood and urine from patients, taken during the disease and injected intraperitoneally into guinea pigs,

readily established, after an incubation period of eight to fourteen days, an infection having a definite clinical course and pathological findings and giving rise to specific immunity.

The clinical picture in the human cases was quite characteristic. The incubation period was fifteen days or less. The onset was acute, with malaise, anorexia, headache, pains in the back and limbs, and fever. These symptoms increased in intensity until the patient became drowsy and stuporous, as in the so-called "typhoid state." The temperature was usually sustained at 102 to 104°F., but sometimes was swinging in character, especially in those who had taken antipyretic drugs. Fever lasted from seven to twenty-four days, with recrudescences in some cases. The pulse was relatively slow. Chilly sensations were the rule, but frank chills often occurred. One patient had a punctate rash on the fourteenth day, but this was not considered to be characteristic. Jaundice, conjunctivitis, vomiting, abdominal distention and constipation occurred in some cases. There was a slight cough in 2 cases. The spleen was not palpable, and enlarged lymph nodes were not made out. The leukocyte counts were normal, but a relative lymphocytosis was noted in most of the cases after the fever subsided. Slight albuminuria occurred in all cases, and was sometimes associated with granular casts. No mention was made of pulmonary involvement or of x-ray studies.

Improvement in symptoms occurred gradually as the temperature fell—usually by lysis. Convalescence varied with the length and severity of the illness. General and persistent weakness was frequent, and in individual cases, residual anemia, nervousness ("nerves"), corneal ulcer or thinning of the hair was noted.

The agent isolated by Derrick on guinea-pig inoculation was studied in great detail by Burnet and his associates,⁹⁸⁻¹⁰² who found it to be pathogenic also for monkeys and mice and possibly for rabbits.⁹⁸ Dogs were found to be susceptible but were not considered to play a part in human infection.¹⁰³ With mice, these authors were able to obtain primary isolations from human material by the intraperitoneal inoculation of blood.^{99, 100} In the spleens of infected mice, they demonstrated typical rickettsia appearing as relatively large intracytoplasmic microcolonies. This rickettsia is fairly large, but is capable of passing a membrane having an average pore diameter of 0.7 micron.⁹⁸ Derrick named it *Rickettsia burneti*.¹⁰⁴ It was found to differ from other rickettsias in that it failed to produce agglutinins for *Proteus* X19 and *Proteus* XK (Weil-Felix reaction) in animals or in man,⁹⁸ and did not give any

cross immunity reactions with other known rickettsias.¹⁰⁵ Like rickettsias, however, it could be grown in tissue cultures but not in bacteriologic mediums.¹⁰¹ Suspensions of this organism were prepared from the spleens of mice and utilized as an antigen that gave specific agglutination reactions with immune serums.⁹⁹ Specific agglutinins appeared in human cases from the twelfth to the fifteenth day after the onset of symptoms, and were also found in animals after infection.⁹⁹

A series of mild and subclinical infections among the laboratory workers was attributed to the handling of infected animals.¹⁰²⁻¹⁰⁶ These infections were usually demonstrated by the development of agglutinins and protective antibodies,¹⁰² but in some cases there was manifest infection and the rickettsias were demonstrated in the blood.¹⁰⁸

Epidemiologic studies revealed a widespread prevalence of the rickettsia of Q fever.¹⁰⁷⁻¹¹³ It was found that the bandicoot, a native rodent of the Australian bush, was susceptible to Q fever, and serologic evidence of latent infection was demonstrated in this species.¹⁰⁷ Later, active infection was proved in these animals by the demonstration of the rickettsia in their blood.¹⁰³ Evidence of latent infection was obtained in other native bush animals, in certain water rats and other native rats, and also in a cow owned by a person who had previously had Q fever.¹¹¹⁻¹¹³

R. burnetii was also obtained from naturally infected ticks collected from bandicoots.¹⁰⁸ It was found possible to infect such ticks experimentally in the larval, nymphal or adult stages by feeding them on infected guinea pigs, and both the latter forms were then capable of transmitting the infection to other guinea pigs.¹¹⁰ There was also suggestive evidence of transovarial passage of the agent in the tick.¹¹⁰ The feces of the infected ticks were found to be highly infectious and capable of infecting guinea pigs when applied either to the abraded or the intact skin. It was considered likely that human beings became infected through this method of transmission.¹¹⁰

Surveys among employees of abattoirs in Brisbane and among foresters working 100 miles from the city showed that the infection was quite prevalent among these workers, the infection, however, was usually latent and demonstrable only serologically. No evidence of infection was found among a group of men in a unit of the militia that had had a short period of training in an area where infected ticks were known to be prevalent. This was interpreted as indicating that these ticks probably do not readily infect human beings.¹¹¹ By the middle of 1940,

145 cases, with three deaths, had been studied by the health authorities in Queensland.¹¹³

American Q Fever

In the spring of 1935, Davis and Cox,¹¹⁴ working in the laboratory of the United States Public Health Service at Hamilton, Montana, described a filter-passing agent obtained from a group of ticks of the species *Dermacentor andersoni* that were collected in a nearby place called Nine Mile Creek. Later, three more identical strains were recovered from the same species of tick collected in southeastern Wyoming.¹¹⁵ This agent produced a characteristic febrile infection in guinea pigs, and the agents could then be obtained and transmitted from the blood and urine of the animals. White rats and white mice were also found to be susceptible, but the infection could not be carried beyond the third transfer in rabbits, and monkeys remained afebrile.¹¹⁴

This agent, like *R. burnetii*, was found to survive in and to be transmitted by nymphal and adult ticks that ingested the agent in the larval stage. It also survived through the eggs deposited by infected females, and was transmitted by the progeny.¹¹⁶ It was found to be a gram-negative, pleomorphic, rickettsialike organism that occurred both intracellularly and extracellularly in affected tissues of the guinea pig. It grew well in tissue cultures and in the developing chick embryo, but not in cell free bacterial culture mediums.¹¹⁷⁻¹²¹

One of the members of the staff of the National Institute of Health in Washington, D. C., visited the laboratory in Montana for a few days in May, 1938, and during this time handled infected animals and worked with tissue cultures of the new agent. Ten days after he returned to Washington, he contracted an illness resembling Australian Q fever. The onset was insidious, with pain in the eyeballs, a "tired feeling" and a slowly rising temperature that reached a peak of about 103°F and later dropped gradually. Chilly sensations followed by mild to moderate chills occurred, and later there was a series of drenching sweats for four nights. There were also pruritis in small joints of two fingers, lasting about three days, at the end of the febrile period. The pulse rate was 90 or lower throughout, and the febrile illness lasted about ten days.¹²²

Blood obtained during the height of the fever and inoculated into a guinea pig produced an infection that resulted in the demonstration of an agent identical with the one isolated in Montana.¹²² This agent was then shown to be closely related to the rickettsia of Australian Q fever.¹⁰⁵⁻¹²³⁻¹²⁷ Cox¹²⁵ suggested the name *R.*

diaporica to emphasize its filterability. No pulmonary signs or symptoms were mentioned.

The American disease was tentatively called "Nine Mile fever," but Cox¹²⁶ later considered the name "American Q fever" preferable. Evidence of the occurrence of this infection was obtained by guinea-pig inoculation, by agglutination tests or by both these methods in persons living in seven different states—namely, Idaho, Montana, Wyoming, Nebraska, Oregon, Nevada and Washington.¹²⁶ Bengston¹²⁸ has developed a sensitive complement-fixation test that is specific for the common rickettsial infections and should be of great value both for diagnosis and for the demonstration of immunity.

An outbreak of so-called "pneumonitis" ascribed to the agent of Q fever occurred among employees of the National Institute of Health in Washington, D. C.¹²⁹ Between March 27 and May 17, 1940, 15 cases occurred among 153 employees of one building, and additional similar mild infections occurred in which x-ray studies either were negative or were not done. One of the patients died. An agent identified as the rickettsia of Q fever was isolated from 3 out of 4 proved cases of pneumonitis, including the fatal case.¹³⁰ Specific agglutinins for the Montana strain and for a strain isolated during the epidemic were found in 9 of 12 proved cases and in 1 of 2 suspected cases. No positive tests were obtained in control serums from workers either in the rickettsia unit or in other units, but a few doubtful results were obtained among the former. Specific neutralizing and complement-fixing antibodies also developed in these cases.^{128, 130} There was no valid evidence that person-to-person contact or the intervention of an arthropod vector was responsible for the transmission of the disease. Although strains of Q fever had been carried in animals and tissue cultures in one unit of the institute since 1938, the personnel of that unit was spared, and the cases were widely distributed throughout the building.

The clinical features and the physical and x-ray findings in these cases were very similar to those of the various atypical pneumonias currently reported from various parts of the United States. The onset was either coryzalike or with headache, chilly sensations and malaise. There was a latent period of three days after the onset, during which headache was severe and constant, but the patients continued to work. In 1 case, there was a dramatic onset, with abdominal cramps, chills, fever and headache while the patient was at work. Chills, fever, sweats, and pains and aches were frequent. Nausea and vomiting occurred in 3 cases. Several patients developed a hacking cough, which in a few cases was productive of thick,

tenacious white mucus, but not "prune juice" or "blood-tinged" sputum. About half the patients had a vague neuralgic type of chest pain that was either substernal or on the side of the lung lesion, but was not pleuritic. All complained of insomnia.

The paucity of physical signs was characteristic. There was no evidence of respiratory embarrassment or any other obvious indication of pneumonia. In some cases, there were areas of dullness or increased breath sounds, or infrequent sticky rales were heard. The pulmonary lesion probably would not have been discovered in most cases except for the x-ray picture. This was the most typical and consistent evidence of the pneumonia. It showed soft, infiltrating lesions, either single or multiple, that were not uniform as in lobar pneumonia but tended to be patchy.¹²⁹

The histopathology in the lungs of the fatal case¹³¹ closely resembled that described by Kneeland and Smetana⁶³ and by Longcope.¹³² Rickettsias were not seen. The spleen showed a picture similar to that found in experimentally infected monkeys¹³¹ and resembled that described in Kneeland and Smetana's⁶³ case. Lesions in the lungs similar to those found in the human case were also described in experimentally infected guinea pigs¹³³ and mice.^{134, 135}

Two similar cases of American Q fever have been reported from Montana.¹³⁶ One patient had typical pneumonitis. Both cases were proved by agglutination tests, and the causative agent was isolated in 1. These infections occurred in the late fall, and both patients had been out in the woods before the onset of symptoms. There was no history of tick bite in these cases, nor was this likely at that time of the year.

Comparative studies of the American strains of *R. diaporica* and the Australian strains of *R. burneti* have been made in both countries and have given fairly uniform results.^{105, 122-124} Immunologically, these strains are indistinguishable. Such differences in pathogenicity as have been noted may be ascribed to the lower virulence of the Australian strains, which has been fairly constant according to all the experimental work.

The clinical differences between the Australian and the American disease have already been commented on in the *Journal*.¹³⁷ Outstanding is the fact that pulmonary involvement or suggestive symptoms of such involvement have not been mentioned in the Australian cases. This may, of course, be due to the lower virulence of the infecting agent in Australia. It is also possible that such lesions have been recognized more easily in this country because of the readiness with which x-ray films of the lungs are made here, particu-

larly in the classes of patients in whom the reported cases have occurred.

The exact place of Q fever in relation to the etiology of the prevalent atypical pneumonias is not yet clear. Except as already noted, no group of proved cases of pneumonia due to this agent has been reported, although many have searched for it. These rickettsias, like the agents of the psittacosis group, may account for only a small percentage of the cases.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28351

PRESENTATION OF CASE

A fifty-year-old woman was admitted to the hospital because of persistent crampy abdominal pain.

Approximately a week before admission, she became constipated and accordingly took a laxative. After this, she developed generalized crampy abdominal pain, which persisted to the time of admission in spite of repeated enemas. These were productive of small stools and great amounts of flatus. There was no vomiting, and no melena or fresh blood in the stools.

The past history was irrelevant, except that the patient has always been somewhat constipated, requiring the frequent use of mild cathartics. Also, for several years she had had slight, irregular metrorrhagia. Her husband stated that for several years she had complained of mild abdominal aches and pains. She ascribed these pains to the onset of menopause, although she was still menstruating. She had been married for thirty-one years and had had four children.

Physical examination revealed a well-developed and well-nourished woman in no acute distress. Examination of the lungs and heart was negative. The abdomen was markedly distended and tympanic. Peristalsis was moderately high pitched but not tinkling. Rectal examination was negative.

The blood pressure was 140 systolic, 70 diastolic. The temperature was 99°F., the pulse 80, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,040,000 with a hemoglobin of 12.4 gm., and a white-cell count of 17,400. The blood Hinton reaction was negative. The nonprotein nitrogen was 24 mg. and the protein 6.1 gm. per 100 cc. The urine examination revealed a specific gravity of 1.026 and a ++ test for albumin, and the sediment contained 200 red blood cells and 15 epithelial cells per high-power field.

A flat plate of the abdomen demonstrated that the colon and small bowel were markedly distended with gas. Most of the gas appeared to be within the colon and extended to the region of the sigmoid.

A proctoscopic examination was performed. The proctoscope was passed 18 cm., where on the

left anterior wall of the sigmoid, just below the level of the cervix, a localized mass was visualized. Biopsy, performed with difficulty because of pressure from a large heavy cervix, was reported as showing acute and chronic inflammation. A biopsy of the cervix showed chronic endocervicitis. During a barium enema, the barium passed very slowly through the terminal 5 cm. of the sigmoid. The lumen of the bowel was considerably reduced, and frequently went into spasm. No definite filling defects or ulcerations were seen. A second proctoscopic examination was performed. The scope passed 18 cm., but further progress was impossible because of inflexibility of the sigmoid due to an extrinsic mass. A good view of the recto-sigmoid was obtained, and no break was found in the mucosa so far as it was exposed. The tumor mass seemed to lie anteriorly and did not involve the cervix.

On the fifth hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. LELAND S. MCKITTRICK: I think perhaps we had better see the x-ray films before starting this discussion.

DR. AUBREY O. HAMPTON: This is the first film, which demonstrates obstruction in the colon. The gas extends down to the sigmoid. The small bowel is more dilated than is usual with a lesion as low as that; it is, nevertheless, only moderately dilated, whereas the colon is markedly so. I am rather surprised that they said this area did not represent a filling defect. I should call it an annular constriction, with a definite filling defect. I do not see the evidence of spasm. That was perhaps observed at fluoroscopy.

DR. MCKITTRICK: This whole picture, to me at least, is difficult to put together logically. The history is short, with a rather sudden onset, and yet the patient came in markedly obstructed, which is unusual, it seems to me, for so short a story. We might try to connect the obstruction in the large bowel with the abdominal aches and pains that she is said to have complained of for several years, but they were quite indefinite, and I do not see how we can put much significance on them.

Metrorrhagia is mentioned, but no vaginal examination is recorded, and I cannot believe the patient did not have an examination.

DR. TRACY B. MALLORY: She had one under anesthesia, and a biopsy of the cervix was done. Evidently the findings were not remarkable.

DR. MCKITTRICK: That is all right. It would be nice to know if she were staining.

There were 200 red blood cells in the urine. How shall I explain that? It seems to me difficult to make all these things fit what I believe is the correct diagnosis.

On the basis of what we know, the patient had something obstructing the sigmoid. She might have had an infiltrating process on the outside that was constricting it, some process within the wall of the bowel itself that narrowed it down, or something within the lumen that caused the obstruction. This woman had had pain for some time, and the abnormal menstrual history makes one wonder if she had an endometriosis that was responsible for the obstruction and menstrual disturbance. I cannot make such a diagnosis with certainty and shall dismiss it. The next possibility is a malignant process in the pelvis, originating in the uterus or ovaries, which had actually extended to the point where it had shut off the bowel. I do not believe it is logical to assume that this occurred.

Then there is regional enteritis or a localized area of ulcerative colitis. These are remote possibilities. A local amebic ulceration, a so-called "amebic granuloma," might be considered, but I do not know how to make such a diagnosis. Diverticulitis should be mentioned, but I do not believe that process would give this picture on proctoscopic examination. Although the x-ray film is often not too accurate at the level of this lesion, it seems quite definite in this case. Sigmoidoscopic examination, too, is sometimes very difficult at this level, particularly if there is fixation of the bowel from something either within or outside the bowel. It would help us greatly in our interpretation if we could be sure—as the examiner stated—that the mass was extrinsic. I do not believe that the pathological report of "chronic inflammation" means anything. We have failed at times to get our specimen from the right place. I must end up by putting my money on the horse that usually wins the race: I must say carcinoma of the rectosigmoid because I do not know what other diagnosis to make. I have not been told anything about the 200 red cells. I do not know what they were doing there, and I shall not make any attempt to explain them.

DR. MALLORY: This patient was operated on because of the severe degree of obstruction. At the first operation, nothing was done but a tube cecostomy, and the bowel was put at rest for nearly two weeks. Then a second operation was done. This time, a fairly thorough exploration revealed a large tumor mass in the region of the rectosigmoid, somewhat adherent to the uterus but movable enough so that it could be resected. It was still considered unwise to attempt a resection at the moment because the bowel contained such large amounts of fluid feces that it seemed

risky. On this occasion, a colostomy was done.

Would any of that information lead you to change your mind?

DR. MCKITTRICK: No, but I suppose you are going to tell me that this was all inflammatory and when the patient came back for operation they did not find anything.

DR. MALLORY: Not so bad as that.

CLINICAL DIAGNOSIS

Carcinoma of rectosigmoid.

DR. MCKITTRICK'S DIAGNOSIS

Carcinoma of rectosigmoid.

ANATOMICAL DIAGNOSES

Endometriosis of uterus and sigmoid.
Intestinal obstruction.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At the final operation, the large tumor mass was again found to involve both the sigmoid and the uterus. For that reason, hysterectomy was first performed, followed by an abdominoperineal resection of the sigmoid and rectum. It was necessary to remove a segment of the posterior vaginal wall as well. When we opened the sigmoid, we found that it contained two intramural tumors that projected into the lumen, separated from each other by 2.5 to 3.0 cm. The mucosa over each tumor was perfectly smooth and nowhere ulcerated. The muscularis was markedly thickened, and one could see very clearly the transverse strands of the muscularis running through the tumor—in other words, there was infiltration of the bowel wall without destruction of the musculature. In several places, there were tiny cystic cavities containing blood. On the posterior surface of the uterus were some firm white nodules looking like tumor implants. On section, each of these nodules contained chocolate fluid, confirming the diagnosis of endometriosis. We have seen endometriosis invade and obstruct the sigmoid before, but I do not believe we have ever seen endometriosis so extensive as this in a woman of fifty. She was still menstruating, however.

CASE 28352

PRESENTATION OF CASE

An eighteen-year-old schoolboy was admitted to the hospital because of a mass in the right thigh.

About three and a half months before entry, the patient was kicked in the thigh while playing football. The resultant slight swelling and stiffness without discoloration lasted only a few days. The injury was then forgotten until a month later,

when the patient noted a firm swelling, somewhat larger than a golf ball, at the site of the former trauma. Following its discovery, this mass grew rapidly. At no time was this lump painful, hot, discolored, numb or throbbing. A month before entry, the patient consulted a physician and was told that he had a "broken blood vessel." There was no loss of weight or fever.

The past and family histories were irrelevant.

On admission, abnormal physical findings were limited to the right lower extremity. In the anteromedial portion of the mid thigh was a firm solid rounded mass 10 cm. in diameter. It was not tender, and could be moved by the examiner or by the patient along with the quadriceps muscles.

The pulse, temperature and respirations were normal.

Examination of the blood showed a white-cell count of 7400 and 100 per cent hemoglobin. The blood calcium was 11.3 mg. and the phosphorus 3.8 mg. per 100 cc., and the phosphatase was 4.2 Bodansky units. The blood Hinton reaction was negative. The urine was normal.

A roentgenogram of the right thigh showed a soft-tissue swelling in the anteromedial aspect of the middle third, with linear areas of calcification within the swollen area. This calcification did not run in the direction of the muscle fibers. A roentgenogram of the chest showed a ring shadow in the right apex, probably an artefact. The lung fields were otherwise clear. The heart seemed normal.

On the third hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CARROLL B. LARSON: The history leads one to think first of all and most strongly of myositis ossificans. A definite injury, severe enough to result in a hematoma, partially subsided, only to be followed by the appearance of another mass at the same site. This places the lesion on a traumatic basis, and it is well known that trauma initiates osteogenesis, although the mechanism of this process is obscure. The location of the mass is one of the three sites of predilection for the occurrence of osteogenesis following trauma—the other two being in the upper extremity about the deltoid muscle and near the attachment of the triceps muscle. Someone has accounted for aberrant osteogenesis in the abdominal wall on the basis of an embryologic rib remnant, which I am sure does not account for osteogenesis in the thigh. The x-ray films show an area of calcification inside the solid tumor that is globular, well defined and completely separate from the femur. The calcification is generalized, with a sprinkling of more localized calcium deposits, so that it has a dotted-

veil appearance that is quite characteristic of myositis ossificans. I do not see that the calcification here follows any definite pattern or direction. An ordinary calcified hematoma gives a different picture and tends to follow fascial planes, for which this mass has no regard, so that I believe we can rule out hematoma.

Malignant tumors must definitely be considered. These might be primary or might originate in a focus of myositis ossificans. In a series of 25 cases of the latter, I definitely malignant case was encountered. This is reasonable, when one considers that the elements of normal bone are present in the bone formed in myositis ossificans, which is therefore subject to the changes of any bone, that is, osteogenic sarcoma, fibrosarcoma, parathyroid changes and so forth. It has been a clinical observation that a diagnosis of malignant tumor in myositis ossificans is difficult, and occasionally must be based on the subsequent course rather than on the microscopic appearance.

I doubt whether we can tell from the history, x-ray films or physical examination whether this mass was malignant; the final diagnosis depends on the histologic structure of the tumor and the future clinical course.

DR. LAURENCE L. ROBBINS: Dr. Larson has pointed out the mass and the calcification. I am sure I cannot tell whether this calcification goes with or against the muscle fibers. One thing that is of some importance, at least so far as the history is concerned, is the fact that in the work done at Dillon Field House, Harvard University, the calcification in cases of myositis ossificans usually appeared within three weeks, and increased from that time on. Judging from these observations, there should be a great deal more calcification in this case than there is; if it was myositis ossificans.

DR. ERNEST M. DALAND: I should like to say that when we pinned this boy down to a more definite history he said that he had been in a football game but was not certain that this was the point where he had been injured. Certainly, there was no hematoma or ecchymosis.

DR. LARSON: I do not believe that rules out myositis ossificans, because in the largest series that I was able to find only 50 per cent of the patients gave a history of injury.

DR. TRACY B. MALLORY: The chief question in a case of this sort, in which it is obviously impossible to make an accurate preoperative diagnosis, is, What would one do about it?

DR. LARSON: I should like to know one more thing, not recorded in the history: Was there any pulsation or any bruit?

DR. MALLORY: No; there was not.

DR. LARSON: In a case like this, hemangioma is perfectly possible but I do not think it likely;

outside the United States, and the participation of South American and Central American physicians in the proceedings contributed greatly to the international character of the meeting. In addition, the presence in the *Journal of the American Medical Association* of a larger number of abstracts of papers appearing in the medical periodicals of these other countries indicates a growing appreciation of medical matters of mutual interest, and a sanitary-engineering survey of South America now under way will undoubtedly lead to further co-operation. Such an interchange of medical thought will undoubtedly contribute much to medical advance.

MEDICAL EPONYM

RAYNAUD'S DISEASE

A. G. Maurice Raynaud (1834-1881) described this disease in a thesis submitted to the Faculty of Medicine in 1862 and entitled *De l'asphyxie locale et de la gangrène symétrique des extrémités* [*Local Asphyxia and Symmetrical Gangrene of the Extremities*] (Paris, 1862: 174 pp.). A portion of the translation follows:

I propose to demonstrate the existence of a kind of dry gangrene affecting the extremities, which it is impossible to explain by vascular obliteration; a kind that is characterized particularly by a remarkable tendency to symmetry, in that it always affects similar parts, the two upper or lower extremities, or all four at once; furthermore, in some cases, the nose and the ears are affected, and I shall endeavor to prove that this species of gangrene is caused by a disorder in the innervation of the capillaries. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY COMMITTEE ON MATERNAL WELFARE

CASE REPORT: OPERATIVE DELIVERY FOLLOWED BY SHOCK AND DEATH

A thirty-six-year-old para III was sent to the hospital. The past history was entirely irrelevant. The two previous pregnancies had terminated normally with living children. The labor of the third pregnancy was long, and after two hours of strong second-stage pains, forceps delivery was attempted at home but was unsuccessful. On admission, the patient was given ether, and a difficult midforceps extraction was accomplished. A living child was obtained. Immediately after delivery, the pulse became very rapid, although

there was no unusual bleeding. The patient was not transfused, but intravenous glucose and stimulants were administered. Death occurred one hour after delivery. An autopsy was not performed, and the death certificate was signed "organic heart disease and cardiac decompensation."

Comment: Since there is nothing in the past history of this patient to suggest organic heart disease and cardiac decompensation, and since no autopsy was performed to confirm this diagnosis, it seems much more probable that death was caused by post-partum shock. In all probability, this fatality was due solely to poor obstetrics. The delivery in the hospital was described as "difficult"; nevertheless, it was successful, and a living child was obtained. It is fair to conclude that had this patient been hospitalized at the beginning of labor, the same operation would not have been difficult several hours earlier, and that shock and death would not have resulted.

DEATH

HOGAN — DANIEL J. HOGAN, M.D., of Roslindale, died August 15. He was in his fifty-sixth year. Dr. Hogan received his degree from Tufts College Medical School in 1920. He was a major in the United States Army Medical Corps, and a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

WAR ACTIVITIES CIVILIAN DEFENSE

INSTRUCTIONAL FILMS

An excellent sound film, "Emergency Medical Service," is now available for medical units. It shows how an emergency medical service operates in co-operation with the other civilian-defense services, and the accompanying sound disk explains clearly the operations of the unit. The showing time is twenty-one minutes.

This film and other very good instructional 16-mm. sound and silent films on first aid, chemical warfare and first aid for gas casualties are available through the Film Department, Speakers' Bureau, Massachusetts Committee on Public Safety, 18 Tremont Street, Boston. These films are loaned to any medical unit that specifies the date on which the films are desired, guarantees the cost of shipment and provides suitable equipment and the services of a competent operator.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JULY, 1942

DISEASES	JULY 1942	JULY 1941	FIVE-YEAR AVERAGE
Anterior poliomyelitis	8	5	9
Chicken pox	436	519	421
Diphtheria	22	9	13
Dog bite	1276	1286	1228
Dysentery, bacillary	0	24	30
German measles	211	116	56

infections. Therefore, it is probably allergic rather than viral in origin. In acute encephalomyelitis, the onset is abrupt, and the involvement widespread. The patients either succumb or recover only to have some residuum. In the latter event, the disease is often diagnosed as multiple sclerosis. But the onset of the latter disease is usually less widespread, and one group of symptoms and signs disappears as others occur. There seems no evidence of a virus etiology for this syndrome.

In conclusion, Dr Merritt pointed out that, from 1928 to 1938 at the Boston City Hospital, 1 in 3680 admissions and 1 in 126 neurologic admissions were for encephalitis.

Dr Thomas then discussed some of the investigative problems. The equine and St. Louis encephalides, although caused by different viruses, may merge during epidemics. At present, there is no way of determining whether these diseases will continue to increase in incidence or disappear, as the Australian X disease did. But whereas equine encephalitis was originally considered solely animal, it and louping ill have become human and may be forerunners of other animal diseases now studied in the laboratory. The classification of virus diseases of the nervous system cannot be based on histologic findings because of their lack of specificity and consistency. Attempts have been made to class them as epidemic and non-epidemic, neurotropic and pantropic, and according to whether their virus etiology is proved, probable or suspected.

Laboratory detection of a virus is difficult, and identification is usually dependent on immune reactions. This may be carried out by injection of the unknown material into animals vaccinated against known viruses, by neutralization of the injected material with various antisera before injection and by some newer *in vitro* methods.

Dr Thomas then considered the epidemiology and immunology of specific diseases. St. Louis encephalitis has been increasing geographically since the first epidemic in 1933, and is often associated with Western equine encephalitis. The virus can be isolated only from the central nervous system in fatal cases, but immunization may be carried out by nasal irrigation in known cases or in infected animals. These late summer epidemics are most *quinto* borne and have their perpetuation in stagnant water. Horses have shown evidence of previous attacks in immune reactions. Antibodies appear in two weeks and persist indefinitely. The virus must be identified in the blood and cerebrospinal fluid for its etiologic role to be proved.

Western equine encephalitis has been increasing in man each summer since 1937. This virus has been isolated from the blood and cerebrospinal fluid in active cases, as well as from post-mortem material. Its presence in ticks, as well as in many animals, birds and mosquitoes, may explain some dry season epidemics. Neutralizing antibodies are found early, whereas complement fixing ones may persist for three years.

Eastern equine encephalitis, known in horses since 1933 and in man since 1938, is immunologically distinct from the Western variety but is transmitted similarly. Its virus has been isolated only from autopsied central nervous system tissue. Neutralizing antibodies have been demonstrated as early as six to eight days.

Other forms of encephalitis are of less practical importance. Australian X disease may be the same or similar to louping ill, but its virus has been lost and the disease seems extinct. Japanese B encephalitis is apparently very similar to the St. Louis type in manifestations and epidemiology.

Russian forest spring fever is carried by a rodent-tick combination. Louping ill, transmitted by a sheep tick, has caused rare cases in laboratory workers. The B virus of the monkey may be responsible for a rare case of fatal ascending myelitis. Lymphocytic choriomeningitis occurs naturally in mice, in which the manifestations, however, are nonspecific. It can be transferred *in utero*. Transmission to human beings can often be traced to recent handling of mice, and even home rodents are not above suspicion as carriers. The virus apparently may enter the intact skin. Insect transmission is possible but of no practical significance as yet.

Von Economo's disease has always been clinically suspected of having a virus etiology, but none of the present known strains have been identified. Similarly, infectious polyneuritis and herpes zoster are considered to be viral in nature, but the responsible agent still escapes detection.

Dr Henry R. Viets opened the discussion by pointing out that there may be multiple invasions by viruses. Strong antibody titers may be observed for as long as seven years. Dr Conrad Wesselhoef stated that one virus activating another may be the mechanism behind certain postinfectious encephalides. Of 4 patients who developed encephalitis during the third week of measles, 3 were found to have the virus of the Eastern equine strain. Post-measles encephalitis is not uncommon, but there are surprisingly few personality changes in relation to the amount of coma accompanying the attack. In mumps, encephalitis may be concurrent or even initiating, as well as occurring during convalescence. In the former event, it is often difficult to rule out the diagnosis of preparalytic poliomyelitis. As many as 800 leukocytes per cubic millimeter may be found even in routine spinal fluids from patients with mumps, which leads to the suggestion that this is really a systemic disease.

BOSTON CITY HOSPITAL

The first of a series of lectures sponsored by the Boston City Hospital House Officers' Association as a preparation for physicians entering the armed forces was given on May 5 at the hospital.

Dr Donald W. MacCollum spoke on "The Practical Management of Burns." He first considered thermal burns. First-aid instruction for the layman should emphasize the care of shock in any burn. If a physician is not present but available, the burned area should be covered with clean linen. In minor burns, the patient may be taken to a first aid post, but in the more extensive cases the doctor should be brought to the patient. Tannic acid ointment should not be applied to any burn at this stage. If a physician is not available for several hours, minor burns should be washed under running water, if that is available, and should otherwise be covered with a paste of sodium bicarbonate and water. The area is then loosely wrapped with an abundant clean handkerchief, and the patient is sent to a doctor. For extensive areas, easily removed clothing is gently removed without further attempts at cleansing, the patient is covered with clean clothes soaked in a warm solution of sodium bicarbonate, kept warm, given tea or coffee by mouth and hurried to a hospital. The important points to be remembered are: tannic acid jelly or strong tea should not be applied to a burn before it has been properly cleaned, grease in any form should be avoided, the patient should not be manipulated unnecessarily in an attempt to apply a neat bandage. First-aid instructions to physicians emphasize the value of examining and treating the patient for actual or in

cient shock before the burn is cared for. For this purpose, the control of pain with adequate amounts of morphine is very necessary, and the dose should be double that usually administered before an elective operation on a patient in shock. In severe shock, oxygen by some method, intramuscular caffeine and plasma, if available, should be given. The last is administered intravenously at the rate of 5 cc. per pound of body weight. In its absence, physiologic saline solution, 10 cc. per pound, may be temporarily given. Only after shock has been combated should the burn be evaluated. If the burn is minor, cleansing is carried out by gentle washing for seven minutes with sponges soaked in 50 per cent solution of green soap (not tincture) and 50 per cent hydrogen peroxide. Débridement is done only with sterile instruments, and the area is then flushed with copious amounts of physiologic saline solution or distilled water, dabbed dry, and dusted with one of the sulfonamide powders. Burns of the hands, feet, face and genitalia are covered with a sterile ointment and bandaged as well as possible. Elsewhere, tannic acid jelly or triple dye may be employed. Splinting should be carried out wherever indicated for the best orthopedic results. In the event of a major burn, only the adherent clothing and the gross contamination, without extensive cleansing, are removed. One of the sulfonamide powders or an emulsion or suspension in a water-soluble base is then liberally applied. If powders are used, they should be covered preferably with a water-soluble jelly, since they are more easily removed than the sterile ointments and triple-dye jelly, which, however, may be used. Thick bandages, to prevent soaking through and further contamination, are applied, with a surrounding pressure bandage if possible, and the victim is hurried to a hospital. The major points in this group are: the shock should be treated before all else; tannic acid ointment should be applied only after the area has been cleansed, and never to the hands, face, feet and genitalia; adequate doses of morphine should be used; the sulfonamide powders should not be allowed to enter the nose and eyes, where they are very irritating; and a very thick bandage should always be applied over extensively burned areas.

Hospital treatment of burns of minor degree is essentially that described above under first-aid treatment by physicians. In major burns, the degree of shock should be checked clinically, and further treatment in the form of heat, morphine and so forth should be administered. If time permits and facilities are available, determinations of the red-cell count, hemoglobin, hematocrit and serum protein are helpful but not necessary. Additional plasma in the amounts recommended above should be given. Whole blood should not be used except when there has been blood loss from other injuries. Anesthesia is employed if indicated, the intravenous or rectal route being chosen if there is any question of hot air or gas inhalation. The area is cleaned and débrided as described above, under sterile precautions. Burns of the hands, feet, face and genitalia are dusted with one of the sulfonamide powders, covered with a sterile ointment and bound with thick layers of gauze, and the extremities are splinted. For burns elsewhere, a similar routine may be carried out only if one is prepared to combat the fluid loss with repeated plasma transfusions. Usually, it is better to employ one of the escharotics to prevent serum loss, but specialized aftercare is probably one of the more essential features of this type of burn. This includes a clean, electrically heated bed, frequent evaluation of the blood chemistry, adequate oral and parenteral fluid intake, and constant medical and nursing care.

The hospital treatment of old burns differs in certain respects from that outlined above. The use of the sulfonamides in the first-aid treatment increases the period during which débridement may be carried out to as long as thirty hours after the burn has been received. Otherwise, this procedure is contraindicated later than eight hours, since the area should be considered already infected. Shock treatment is still the first consideration. The patient is then immersed in a tub of warm tap water, with constant exchange of water for several hours. After gentle drying, the sulfonamide powder of choice is used and is followed by a sterile ointment. Tannic acid in any form is contraindicated. If the burn is crusted, the area may be first covered with what some consider the dressing of choice in old burns, namely, wet saline or *tulle gras* with Eusol—a chlorinate compound made of slaked lime and sodium bicarbonate.

Grafting should not be necessary in second-degree burns, and in deeper ones the kind and amount of graft depend on the extent and site of the burn. Special preoperative precautions are taken to have the patient in the best possible condition generally and locally. The important conditions for successful results are to have the granulations cleaned at least to their fibrous base, which in cases of contractures should be removed. Island or Reverdin grafts should be strictly avoided for the best cosmetic results and for the shortest convalescence.

The second large group of burns are those caused by chemicals. The first warning here is for the attendant to protect himself. Mustard gas is really a fine oily vapor, and the exposed areas must be attacked early. All clothes are removed and decontaminated. Then, the victim is given a thorough soap-and-water scrub, followed by shaving of hairy regions if they have been affected, for they are not otherwise easily cleaned and may develop subsequent burns. If this is done in less than a few hours, there is no need for further treatment, but the patient should be observed temporarily. In patients seen after eight hours, the burned areas are treated like any old burn. One should always consider the possibility of damage to the pulmonary structures if anesthesia is contemplated, and morphine for shock should be avoided for this same reason.

Treatment of exposure to lewisite liquid is of no value after one minute. Within that time, the area should be bared of all covering, and the wound repeatedly swabbed with hydrogen peroxide, which is continued for half an hour. The area is then washed for seven minutes with soap and water, and an alcohol pad is applied and left in place for five minutes. A dry dressing is applied, and if no blister appears in twelve hours, the patient may be discharged. If blisters develop, they are then treated carefully, so that none of the fluid escapes onto the surrounding skin, for it contains the same arsenical as the original fluid and will cause grave injury. Even a small amount of this material will be fatal if it reaches the blood stream through any route. If blisters have broken and the patient shows signs of arsenical poisoning, the entire area is widely excised, and immediate graft carried out. Sodium thiosulfate is the drug of choice in combating systemic poisoning.

Phosphorus has the peculiar property of continuing to burn even after being imbedded in the flesh. If there is none still active, the area may be treated as a thermal burn. But if bits of the material are smoldering on or in the skin, the region must be kept wet, preferably with warm water. Five to 15 per cent copper sulfate may be applied if available, for it will temporarily stop the burn.

ing But the phosphorus particles must be removed by some method before the patient can be considered out of danger Thereafter, the treatment is the same as that for any burn

Acids and alkalis, contrary to popular belief, should not be neutralized, for in that way the heat generated or the neutralizing agent may cause a burn It is preferable to use continuous running water or to immerse the victim in a tank or nearby body of water The only exception to this is that excess lime is wiped off before wetting

Electrical burns are deceptive from the first One should not be overzealous in attempting to remove a patient from the scene before first determining that the current has been disconnected or that the rescuer is properly insulated The patient should not be regarded as dead until rigor mortis sets in, for several cases are reported of recoveries after many hours without a perceptible heart beat Almost all these burns are third degree or more because of the intense heat and coagulation of the blood in the vessels supplying the area Coagulation may cause slough on the seventh to tenth days, sometimes with hemorrhage The area is treated like any burn except that no eschars are applied, and daily dressings are done to follow the progress of the slough if there is any Sloughed areas are not surgically removed but are allowed to separate for the amount of tissue thus lost is much less than would have been computed at an earlier stage Sterile hemostats and a tourniquet should always be at the bedside, to guard against the danger of hemorrhage at the time of separation of the slough

BOOK REVIEWS

Allergy in Clinical Practice By staff members of the Cleveland Clinic Under the direction of Russell L Haden, M.D., chief of the Medical Division Edited by J Warrick Thomas, M.D., chief of the Section on Allergy 8th, cloth, 370 pp, with 92 illustrations, including 14 in color Philadelphia J B Lippincott Company, 1941 \$5.00

This book is an endeavor to present the various phases of allergy as applied to general practice The well known manifestations of allergy with reference to the upper and lower respiratory systems and skin receive major emphasis, with some consideration of the less common reactions on the gastrointestinal, ocular and endocrine systems The presentation is orderly and marked by clarity and brevity In fact, if what appears to be a disproportionately large number of illustrative case reports were considerably reduced, one would be left with a concise monograph summarizing the general principles of allergy without appreciable loss of practical value

The Advancing Front of Medicine By George W Gray, AB 8th, cloth, 425 pp New York Whittlesey House 1941 \$3.00

It is a task of no little difficulty to present matters of scientific research to the public so that they are readily understandable, to convey the facts with accuracy and the significance of those facts with clarity But Mr Gray has achieved it here with almost astonishing perfection He has done it, moreover, without resorting to the false sensationalism that so often offends in similar pieces of reporting And the more, because he is an outsider looking in, does one marvel at his restraint and judgment

But Mr Gray's front should really be fronts He has chapters on the nature of disease, on heredity, on the vitamins (on which the public has been so perniciously exploited), on the blood and its disorders, on hypertension, on the sulfonamide drugs, on influenza, on allergy, on the relation of anxiety to health, on epilepsy and certain other nervous disorders, on sleep, on pain and its relief, on drinking, smoking and drug addiction, on cancer and on growing old

With its wide range, its sane way of weighing and balancing and its bits of history, this book is revealing even to a physician, how much more so, then, to the layman, to whom nearly all its matters must come as something fresh and new Perhaps its selection by the Scientific Book Club will increase its circulation, it deserves a wide one, for it is capable of doing a great deal of good

Diseases of Women By Harry S Crossen, M.D., and Robert J Crossen, M.D Ninth edition, entirely revised and reset 4th, cloth, 962 pp, with 1127 engravings, including 45 in color St Louis The C V Mosby Company, 1941 \$12.50

This is the ninth edition of a very familiar textbook on diseases of women The greatest advances that it heralds are those of endocrinology and chemotherapy The former has imposed on the whole field of gynecology a physiologic approach in place of the anatomic and pathologic As a result, one gets a picture of a changing and cyclic rather than a static group of organs The adaptation of the newer hormoneology to clinical use has been well treated by the authors There is a scarcity of information about stilbestrol, which might well be explained by the rather recent release of this drug by the Council of Pharmacy and Chemistry of the American Medical Association

This is not an operative book, but rather a treatise on diagnosis and therapy Preparation for operation and postoperative care are discussed, but the technique of surgical steps is not included Because of the scope of this work, one hesitates to single out any particular portion for special comment However, the sections on pessaries, endometrial biopsy and the Rubin test are examples of the fine detail that makes this study so valuable to the practitioner

The book will prove most useful to the physician who requires a one volume reference on the problems of gynecology

NOTICES

AMERICAN BOARD OF OPHTHALMOLOGY

Because of the war emergency, the American Board of Ophthalmology announces the following additional examinations New York City, December 13 to 16, and Los Angeles, January 15 and 16

At the last meeting, it was decided to cancel the 1943 written examination, to include in the oral examination all the subjects previously covered by the written examination and to dispense temporarily with the requirement of case reports The oral examination will probably require two or three days and will cover the following subjects external diseases (slit lamp), ophthalmoscopy, histology, pathology and bacteriology, ocular motility, refraction and retinoscopy, practical surgery, anatomy and embryology, perimetry, therapeutics and operations optics and visual physiology, and relation of the eye to general diseases

Formal application on the proper blanks for the December and January examinations must be filed with the secretary not later than November 1. Blanks may be obtained from the American Board of Ophthalmology, 6830 Waterman Avenue, St. Louis, Missouri.

YALE UNIVERSITY SCHOOL OF MEDICINE

A postgraduate course on industrial health and medicine in wartime will be given at Yale University School of Medicine on Wednesday afternoons from October 7 to December 23. Under the auspices of the Departments of Pharmacology, Preventive Medicine and Public Health, lectures and seminars will be presented by Drs. W. F. Von Oettingen, Leroy U. Gardner, R. A. Kehoe, Alice Hamilton, Louis Schwartz, Robert S. Goodhart, George R. Cowgill, C.-E. A. Winslow, M. I. Hall, Lydia Giberson, Louis Sachs, A. B. Landry and A. S. Gray; Lieutenant Colonels A. J. Lanza and D. B. Dill; and A. L. Coleman, Everett Martin, B. F. Postman, J. J. Bloomfield and E. P. Chester.

A registration fee of \$10.00 will be charged, and those who attend the course regularly will be given a statement to that effect. Physicians who are interested may obtain detailed information from Dr. W. T. Salter, Yale University School of Medicine, New Haven, Connecticut.

LEWIS CASS LEDYARD, JR., FELLOWSHIP

The Lewis Cass Ledyard, Jr., Fellowship was established in 1939 by a gift from Mrs. Ruth E. Ledyard, wife of the late Lewis Cass Ledyard, Jr., a governor of the New York Hospital. The income, amounting to approximately \$4000 annually, will be awarded to an investigator in the fields of medicine and surgery, or in any closely related field. This amount will be applied as follows: \$3000 as a stipend and, approximately, \$1000 for supplies or expenses of the research. In making the award, preference will be given to younger applicants who are graduates in medicine, and who have demonstrated fitness to carry on original research of high order. The recipient of this fellowship will be required to submit reports of his work under the fellowship, either at stated intervals or at the end of the academic year; and when the result of his work is published, he will be expected to give proper credit to the Lewis Cass Ledyard, Jr., Fellowship. The research work under this fellowship is to be carried on at the New York Hospital and Cornell University Medical College. The fellowship will be available on July 1 at the beginning of the academic year. Applications for the year 1943-1944 should be in the hands of the Committee by December 15. It is expected that the award will be made by March 15, 1943.

Application for this fellowship should be addressed to: Committee of the Lewis Cass Ledyard, Jr., Fellowship, The Society of the New York Hospital, 525 East Sixty-eighth Street, New York City.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, AUGUST 30

MONDAY, AUGUST 31

12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, SEPTEMBER 1

12:15-1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

WEDNESDAY, SEPTEMBER 2

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

SEPTEMBER 9-12. American Congress of Physical Therapy. Page x, issue of May 14.

SEPTEMBER 29, 30 AND OCTOBER 1. Connecticut Clinical Congress. Yale Law School Building, New Haven, Connecticut.

SEPTEMBER 30-OCTOBER 10. Conference and Course in Legal Medicine. Mallory Institute of Pathology, Boston City Hospital. Page ix, issue July 23.

OCTOBER 7-DECEMBER 23. Yale University School of Medicine. Not above.

OCTOBER 12-23. 1942 Graduate Fortnight. New York Academy of Medicine. Page xi, issue of May 21.

OCTOBER 14-17. American Academy of Physical Medicine. Hotel Statu Boston.

OCTOBER 19-23. 1942 Clinical Congress of the American College of Surgeons. Page ix, issue of February 5.

OCTOBER 21-24. Conference on Venereal-Disease-Control Needs in Wartime. Page ix, issue of August 20.

NOVEMBER 17-20. American College of Surgeons. Page ix, issue August 20.

FEBRUARY 13. American Board of Obstetrics and Gynecology. Page ix, issue of July 2.

APRIL 12-16. American College of Physicians. Page x, issue of July 2.

DISTRICT SOCIETIES

BRISTOL SOUTH

DECEMBER 3. Fall River.

MAY 6. New Bedford.

FRANKLIN

SEPTEMBER 8.

NOVEMBER 10.

JANUARY 12.

MARCH 9.

MAY 11. Annual meeting.

All meetings are held at 11:00 a.m. at the Franklin County Hospital Greenfield.

MIDDLESEX NORTH

OCTOBER 28.

JANUARY 27.

APRIL 28.

JULY 28.

PLYMOUTH

OCTOBER 15. Moore Hospital.

NOVEMBER 19. Plymouth County Hospital.

JANUARY 21. Brockton Hospital.

FEBRUARY 18. Jordan Hospital, Plymouth.

MARCH 18. Goddard Hospital.

APRIL 15. Bridgewater State Farm.

MAY 20. Lakeville.

WORCESTER

SEPTEMBER 9. Belmont Hospital, Worcester.

OCTOBER 14. Rutland State Sanatorium, Rutland.

NOVEMBER 11. Grafton State Hospital, North Grafton.

DECEMBER 9. Worcester City Hospital, Worcester.

JANUARY 13. St. Vincent Hospital, Worcester.

FEBRUARY 10. Worcester State Hospital, Worcester.

MARCH 10. Memorial Hospital, Worcester.

APRIL 14. Hahemann Hospital, Worcester.

MAY 12. Annual meeting.

WORCESTER NORTH

OCTOBER 28.

JANUARY 27.

APRIL 28.

JULY 28.

(Books Received on page ix)

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SIX YEARS' EXPERIENCE OF THE THYROID SERVICE AT THE MASSACHUSETTS MEMORIAL HOSPITALS*

HOLLIS L. ALBRIGHT, M.D.,† AND HOWARD M. CLUTE, M.D.‡

BOSTON

THE Thyroid Service, which was established at the Massachusetts Memorial Hospitals in January, 1936, includes representatives of the associated specialties of otolaryngology and ophthalmology, as well as internists, cardiologists and surgeons. Up to January 1, 1942, the four surgeons on the Thyroid Service, the rotating residents and house staffs have performed three hundred and thirty-four thyroid operations on 288 patients, with 6 deaths, only 1 death having occurred in the last three years (Table 1). The operative mortality was 1.8 per cent, and the patient mortality 2.1 per cent. A review of the operative results has been of value, especially to the surgeons who have served on the hospital and outpatient thyroid services throughout this six-year period, in a realization of what has or has not been accomplished and of plans for future betterment.

Of the entire series, the ratio of females to males was 5.3:1. The youngest patient (exophthalmic goiter) was fifteen years old, and the oldest (carcinoma) seventy-one. Figure 1 shows the age distribution by decades for the toxic and nontoxic groups. As one would expect, exophthalmic goiter is a disease of youth, and nodular goiter one of older patients.

HYPERTHYROIDISM

Exophthalmic Goiter

One hundred and seventy-six operations were performed on 139 patients, with 3 fatalities, the operative mortality being 1.7 per cent. There were 105 females and 32 males, a ratio of 3.3:1. Eighteen of the 30 thyrocardiac cases occurred in the exophthalmic group (Table 1). A patient is described as thyrocardiac when he presents evidence of underlying cardiac damage associated

with hyperthyroidism. Rheumatic, hypertensive and syphilitic heart diseases are most commonly found to be the cause of this damage. Impairment of the cardiac reserve is usually manifested by the presence of preoperative auricular fibrillation or cardiac decompensation, or both. These patients are much more serious operative risks, and all 18 were subjected to a two-stage thyroidectomy, with an interval of six weeks between operations. Two of the three deaths in the exophthalmic group occurred in known thyrocardiac patients, both after the first-stage hemithyroidectomy.

Experience has convinced us beyond doubt that subtotal thyroidectomy in the patient who is a poor risk may be too strenuous a procedure for him to withstand. This is especially true on a teaching service, where the operation may occasionally be prolonged. Therefore, objective evaluation of the patient on the basis of age, weight loss, duration of disease and response to treatment§ was adhered to in the selection of the operative procedure for each patient. Thus, in the exophthalmic group, 37 per cent of the patients were subjected to a two-stage thyroidectomy. All 3 fatalities in the exophthalmic group occurred during the first three years of the Thyroid Service, and after a first-stage hemithyroidectomy, an indication that all the patients were evaluated preoperatively as serious risks.

Twelve patients developed sufficiently severe postoperative reactions to be classified as suffering from thyroid storm, which, on the Thyroid Service, means the presence of a progressively rising fever and a rapid pulse rate, with or without irregularity, in addition to restlessness, delirium, pulmonary congestion and, in cases that cannot be controlled, a fatal ending. Again, on the basis of objective findings, all 12 patients had given enough preoperative warning, so that only a hemi-

*From the Department of Surgery, Boston University School of Medicine and the Massachusetts Memorial Hospitals.

†Instructor in surgery, Boston University School of Medicine; surgeon, Massachusetts Memorial Hospitals.

‡Professor of surgery, Boston University School of Medicine, surgeon-in-chief, Massachusetts Memorial Hospitals

§Clute, H. M. Operative mortality in hyperthyroidism. *J. A. M. A.* 95:387-392, 1930.

in an attempt to arrest the uncontrolled hyperthyroidism. Viewed in retrospect, either preliminary bilateral superior-pole ligation or, even better, a much longer preoperative period might have favorably altered the outcome. The patient had received iodine for one month before admission, and this was perhaps a factor in the poor response to the preoperative management of her hyperthyroidism.

CASE 2. Mrs. S. T., a 69-year-old widow, was admitted to the Evans Memorial on October 13, 1937, complaining of extreme nervousness and rapid onset of the cardinal symptoms of hyperthyroidism during the previous 3 weeks. She had lost 15 pounds during this time, a total of 43 pounds in a year. For 3 weeks, there had been marked palpitation, dyspnea and weakness. There was no ankle edema or chest pain.

Examination revealed an undernourished woman who was nervous and worried, and showed mild activation. The skin was warm and moist. There was no exophthalmos. There was a fine tremor of the extended tongue and fingers. The thyroid gland was symmetrically enlarged to one and a half times the normal size. In addition, a coincidental, discrete 2.5-cm. adenoma was palpated in the right lobe. The heart was slightly enlarged, and the rhythm was regular. However, on the day following admission, paroxysmal auricular fibrillation was noted, and this continued throughout the preoperative course. The blood pressure was 140/78.

The basal metabolic rate was +35 per cent. A photometer reading showed a moderate deficiency in vitamin A. The patient was put on large doses of vitamin A for 15 days, without any real effect on the metabolism, but with marked improvement of the photometer reading. She was then given Lugol's solution, 10 minims three times a day, beginning on the 19th day. On the 36th day, the basal metabolic rate had fallen to -2 per cent (after 17 days' treatment with Lugol's solution). The patient was transferred to the Thyroid Service on the 38th day after admission, when slow auricular fibrillation and moderate cyanosis were evident. She was seen by the cardiologist, Dr. Ashton Graybiel, who considered the cardiac reserve adequate and believed that the patient should be fully digitalized preoperatively. This was done during the next 16 hours.

A first-stage hemithyroidectomy was carried out on November 23, 1937, under cyclopropane and oxygen anesthesia. The patient's condition was satisfactory during the initial stages, and she continued to fibrillate at a slow rate, 50 to 80 beats per minute. The blood pressure, which was 136/94 the day before operation, rose to 184/84 at the beginning of anesthesia and to 214/140 after 10 minutes; the pulse rose to 116. After 14 minutes of operating time, the patient suddenly stopped breathing and became pulseless. In spite of artificial respiration, she could not be revived and died before completion of the operation.

Post-mortem examination revealed no gross, obvious cause of death. The thyroid gland was diffusely hyperplastic. The lungs were essentially normal. The heart showed slight dilatation, and the myocardium was notably soft and flabby. The coronary arteries were sclerosed, with marked fibrous thickening of the intima, in places amounting to almost complete occlusion. Acute cardiac decompensation and acute dilatation of the heart were regarded as the causes of death.

The patient was obviously a very serious risk. She was sixty-nine years old and had lost a large amount of weight (43 pounds) over a period of one year. Latent hyperthyroidism had probably been present for a much longer period than the three weeks of obvious hyperthyroidism. Limited cardiac reserve and actual cardiac damage were present, as shown by auricular fibrillation, dyspnea and palpitation. In retrospect, three questions arise. Would some other anesthetic have been less severe on the patient, would a more conservative operation in the form of pole ligation have been preferable, or should we have taken much longer in our preoperative preparation? In the great majority of serious-risk patients, it is our opinion that the operation can be brought to a speedier conclusion, with less trauma to the patient, under general anesthesia in the form of cyclopropane and oxygen administered by an experienced physician anesthetist. Perhaps, initial ligation of the superior thyroid vessels, first on one side and then on the other, followed by a two-stage hemithyroidectomy, would have helped this patient. In the light of our past experience, single-pole ligation has often failed to arrest the progress of the disease, because of the marked collateral vascularity of the thyroid gland. Consequently, we have placed greater reliance on adequate, rigidly careful preparation of the serious risk patient for a quick hemithyroidectomy. Actually, this has given us greater assurance in arresting and controlling the hyperthyroidism. The questions of whether this patient could have survived four planned, graded, operative procedure or should have had longer preoperative care can not be answered.

CASE 3. W. M., a 53-year-old dyer, was admitted to the hospital on November 3, 1938, complaining of increased irritability, nervousness and a loss of 34 pounds in 1 year. Symptoms including crying spells were severe for 3 months and iodine (5 drops three times a day) had been taken for 12 months before admission. Dyspnea, orthopnea and ankle swelling had been noted for 2 weeks. One brother had died of "goiter" at the age of 34 years.

Examination revealed an 118-pound man who was excited, mentally confused, indifferently co-operative and unreliable in history. There was exophthalmos of the right eye only. The thyroid gland was firm and symmetrically enlarged to three times the normal size. There was no heart disease.

The basal metabolic rate was +53 per cent on admission, and 14 days later +16 per cent. However, the patient lost 5 additional pounds during that period.

Sixteen days after admission, a right hemithyroidectomy was performed, without incident. The course was uneventful for 24 hours, when a temperature of 103°F. and auricular fibrillation at the rate of 130 beats per minute developed. The patient responded well to intensive supportive

therapy until the afternoon of the 2nd day when his temperature rose to 106°F. Ice packs and sodium amylal by rectum produced temporary improvement, without evidence of cardiac failure. However, the patient died suddenly that night, 61 hours after operation, of uncontrolled thyroid crisis. Autopsy revealed bronchopneumonia and pulmonary edema, but no other cause of death.

Adenomatous Goiter with Hyperthyroidism

Forty-seven operations were performed on 40 patients, with 2 deaths, giving an operative mortality of 4.3 per cent. The youngest patient was twenty-five years and the oldest seventy years of age. Twenty-nine patients were over and 11 under forty years. There were 36 females and 4 males, a ratio of 9:1. Many of these patients had had asymptomatic goiter for years, the longest duration being forty years. Relief was sought only when complications, especially hyperthyroidism, appeared. Thyroidectomy was performed in two stages on 7 patients, or 18 per cent of the cases.

Pathological examination disclosed areas of secondary hyperplasia in the multiple colloid adenomatous goiter in 26 cases. In the remaining 14 cases, multiple colloid adenomatous goiter was reported, with associated fetal or embryonal adenomas in 3 cases, secondary hemorrhages in 3 and associated simple adenomas in 4. These 14 patients were considered to have so much clinical evidence of hyperthyroidism that they were so classified, even though the pathological examination did not disclose substantiating hyperplasia.

There were 9 thyrocardiac patients, and 1 death occurred in this group. Another patient developed postoperative thyroid crisis, terminating in death after forty hours. Two patients recovered from impending crisis. Three patients had transient auricular fibrillation postoperatively.

Four hours after operation, the one postoperative hemorrhage of the entire series occurred in this group. Secondary operation for control of the hemorrhage was followed by uneventful recovery. One patient had transient immobility of the left vocal cord that cleared in two months. One patient sustained permanent injury to the left vocal cord, which was present thirty-seven months later. There was no case of bilateral nerve injury in the entire series. No patients were known to have developed recurrent hyperthyroidism, hypothyroidism, myxedema or hypoparathyroidism.

The 2 fatal cases are reviewed below.

CASE 4. G. G., a 67-year-old man, was admitted to the hospital on November 25, 1936, with a swelling of the neck that had been present since childhood and had shown gradual growth in the preceding 12 years. For 6 months increased warmth, marked tremor of the hands and extreme weakness had developed with no loss of weight. The neck had become smaller, that is, a size 20 collar

became too large, suggesting descent of the goiter into the upper mediastinum.

Examination revealed a 168 pound, well-preserved man showing definite activation, with tremor of the extended tongue and fingers. The thyroid gland on the left was replaced by a nodular mass five times the size of the normal lobe; the right lobe was smaller but enlarged. The trachea was deviated to the right with moderate compression. The heart showed no gross enlargement. The pulse rate was 100.

The basal metabolic rate was +31 per cent, and 11 days later, it was +19 per cent. Two days before operation, the pulse rate rose to 148, and auricular fibrillation developed. The patient was digitalized, 15 gr being given over the 2-day period before operation.

A first stage hemithyroidectomy was done 3 weeks after admission. The next day, the patient's condition was considered very satisfactory, with the pulse regular at 70 beats per minute, and the temperature 100.6°F. That afternoon, 90 minutes after an intravenous infusion of 750 cc of 10 per cent glucose and Lugol's solution 10 minims in physiologic saline solution, the patient developed a chill, became cyanotic and fibrillated. Respirations rose to 35 per minute. Despite oxygen and uninterrupted digitalis therapy, the temperature rose steadily to 104°F by axilla, and the patient became semicomatose, pulmonary congestion developed, without edema. He died 40 hours after operation.

The cause of death was regarded as postoperative thyroid crisis leading to failure of first the pulmonary and then the general circulation. No definite opinion could be formed concerning the possible precipitating effect of the intravenous infusion. Autopsy revealed no significant local changes and substantiated the clinical impression of the cause of death.

A review of the preoperative management of this patient brings to the fore the sudden development of auricular fibrillation for the first time two days before operation. This certainly gave a further warning of the serious risk involved in this patient. A longer period of digitalization and cardiac therapy might have averted the fatal outcome. From this and other experiences, we believe that when digitalization is carried out, a delay of several days in operation should follow.

CASE 5. Mrs. A. S., a 61-year-old woman, was admitted to the hospital on November 26, 1941, with goiter for 20 years and symptoms of hyperthyroidism for 8 months. Lugol's solution, 15 minims daily for 6 months, had been attended by temporary improvement followed by progressively severe hyperthyroidism. The patient had lost 15 pounds in the previous year.

Examination revealed a thin, activated elderly woman in the iodine fast state of hyperthyroidism. The thyroid gland was nodular and enlarged to four times the normal size on the right and slightly less on the left.

The basal metabolic rate was +48 per cent, and 8 days later was +46 per cent. The pulse rate ranged from 76 to 128, and on the morning of operation was 76.

Twelve days after admission, a right hemithyroidectomy was done without difficulty. Six hours later, the temperature rose to 105°F, and the classic picture of thyroid crisis developed. On the 2nd postoperative day, auricular premature systoles were disclosed by electrocardiogram. The pulse rose to 200 per minute, and the temperature

ranged from 103 to 105°F.; coma and death occurred on the 3rd postoperative day.

The cause of death was uncontrolled hyperthyroidism; post-mortem examination disclosed no other cause.

Recurrent Hyperthyroidism

Twenty operations were performed on 18 patients who had had previous operations for hyperthyroidism. There were no deaths. Five patients were considered to have persistent hyperthyroidism following operation within the previous two years. The remaining 13 patients had been free from symptoms for from two to twelve years; these were regarded as patients with recurrent rather than persistent hyperthyroidism. All patients appearing for secondary operations for the control of hyperthyroidism have been grouped under the single term "recurrent," however, for the management of both the persistent and truly recurrent cases is identical.

Sixteen patients originally had diffuse goiter of the exophthalmic type, confirmed pathologically as primary hyperplasia of the recurrent remnant. Only 2 showed recurrent nodular goiter with secondary hyperplasia of the remnants.

Fifteen patients had a one-stage reoperation. Two had divided reoperations at six-week intervals. One patient required two reoperations, twelve and thirty months, respectively, after the original thyroidectomy for exophthalmic goiter. There were 3 thyrocardiac patients, in all of whom only single-stage reoperation was necessary.

Preoperative examination of the vocal cords, although desirable in all patients undergoing thyroidectomy, is especially so in those on whom reoperation is contemplated. One patient had paralysis of the left vocal cord following thyroidectomy thirty-seven months previously. Such information aids greatly in averting possible further damage and bilateral vocal-cord paralysis.

None of these patients developed postoperative hemorrhage, thyroid crisis or recurrent-laryngeal-nerve injury. One patient, who developed clinical tetany from hypoparathyroidism on the fourth postoperative day, had had two operations for exophthalmic goiter, eight and seven years previously. Two months after the onset of mild tetany, she was adequately controlled on a regime of calcium and dihydrotachysterol (AT 10), but continued therapy was necessary. One patient developed hypothyroidism and myxedema a year after operation.

NODULAR GOITER WITHOUT HYPERTHYROIDISM

All 74 patients in this group were subjected to single-stage thyroidectomy, and there were no fatalities. Many of the goiters were described as

subclavicular and substernal in position, and several as intrathoracic. However, none were so truly intrathoracic as to require splitting of the sternum or to cause undue technical difficulty of removal through the usual thyroidectomy approach.

The distribution of the pathologic types encountered is presented in Table 3. Much emphasis

TABLE 3. Summary of Cases of Nodular Goiter without Hyperthyroidism.

YEAR	TOTAL NO. OF CASES	DIAGNOSES		
		MULTIPLE COLLOID ADENOMATOUS GOITER	SIMPLE ADENOMA	FETAL ADENOMA
1936	3	1	2	0
1937	12	6	6	0
1938	16	5	9	2
1939	16	9	6	1
1940	9	5	3	1
1941	18	8	10	0
Totals	74	34	36	4

has been laid on the parenchymatous, embryonal or fetal adenoma as representing a true tumor type, in contrast to the colloid or simple adenoma. The parenchymatous adenoma was found in only 4 patients, and the colloid adenoma in 36—nine times more frequently.

The postoperative complications were limited to one permanent and one transient unilateral recurrent-laryngeal-nerve injury that cleared in ten weeks. One patient developed coincidental catarrhal jaundice on the third postoperative day. No deaths occurred.

CARCINOMA OF THYROID GLAND

Seven patients with thyroid carcinomas were operated on during this six-year period. In 5 cases, radical thyroidectomy was carried out, but in none were the cervical lymph nodes or internal jugular vein removed. The remaining 2 patients were subjected to biopsy only, and 1 of these died of myocardial failure on the eighth postoperative day. The surviving 6 patients received postoperative x-ray treatment.

A fifty-one-year-old patient who showed clinical hyperthyroidism associated with unsuspected carcinoma had had symptoms of hyperthyroidism for eight months, with a loss of 12 pounds and an initial metabolic rate of +50 per cent. A subtotal thyroidectomy was done for exophthalmic goiter. However, pathological examination revealed papillary adenocarcinoma in one portion of the diffuse primary hyperplasia seen throughout. The metabolism was -6 per cent seven days later. Examination twenty-six months later revealed the patient to be symptom free, with no signs of recurrence.

Except for the 1 fatality, which is reviewed below, there were no complications. The 6 sur-

viving patients have remained symptom free for four to twenty six months after operation

CASE 6 Mrs A A, a 71 year old housewife, was admitted to the hospital on February 4, 1938, having noted swelling of the left side of the neck for 6 weeks. She had lost 35 pounds and had noted hoarseness for 3 weeks. The swelling grew constantly larger and more painful during this short period.

Examination revealed a well preserved woman with normal findings except for hoarseness and the swelling of the neck. The left lobe of the thyroid gland was enlarged to four times the normal size, the mass was hard and fixed, and involved the isthmus. The right lobe was not palpably enlarged. There were several hard, cervical lymph nodes, 1 cm in diameter, on the right. The trachea was displaced to the right. General arteriosclerosis was evident.

Biopsy of the thyroid gland was performed 10 days after admission. The pathologist reported a rapidly growing exceedingly anaplastic, embryonal tumor, probably of thyroid origin. From the 2nd postoperative day, the patient developed progressive signs of myocardial failure, and succumbed on the 8th day after operation. No autopsy was performed.

The problem of managing the patient with a solitary thyrogenic metastasis of the skull has arisen once in this series. Active intervention, with removal of the long standing calcified malignant adenoma of the right thyroid lobe, followed by craniotomy and removal of the skull metastasis, was carried out. No further recurrence had appeared twelve months after operation.

RARER CONDITIONS

Three patients were seen with parathyroid adenoma, profoundly altered calcium metabolism and bone changes. One was moribund on admission. Excision was carried out on the remaining 2 cases. One patient survived and made a striking, sustained recovery. These records are being prepared for publication.

The congenital anomalies were few in this series. Lateral aberrant thyroid tissue was removed from the neck in 2 cases. Persisting remnants of the thyroglossal duct were also removed from 2 patients. No patients with lingual thyroid tissue were seen. No complications and no deaths occurred in this group.

SUMMARY

A six year review of the Thyroid Service at the Massachusetts Memorial Hospitals is presented. Since this is a general ward service, many of the seriously ill patients first appeared in advanced untreated stages of thyroid disease. They showed evidences of dietary deficiencies and constitutional disease. In the treatment of such patients, our experience has justified, we believe, the relatively high rate of divided operations (31 per cent) in the 197 patients with hyperthyroidism. In spite

of this conservative approach, a thyroid crisis developed in 16 of these 197 patients, 4 of whom died. It is apparent that in a ward thyroid service, therefore, one must take a longer time and give more detailed care in the preoperative preparation of patients with hyperthyroidism if the same low mortality figure as that among private patients is to be obtained.

The morbidity and mortality rates have been constantly kept before us in our efforts to improve these results. Although the mortality rate of 17 per cent among patients with exophthalmic goiter conforms with results generally obtained, it is interesting that no patient died of this disease during the last three years.

The patients having adenomatous goiter with hyperthyroidism showed a mortality of 4.3 per cent. There were 2 deaths in the 40 cases, both due to thyroid crisis. Associated cardiovascular impairment was present in 23 per cent of these cases, whereas only 13 per cent of the exophthalmic group showed this complication. These patients were on the average much older than the exophthalmic patients, and the goiter was of long standing.

There was no mortality in the eighteen secondary operations for recurrent toxicity.

The four permanent, unilateral recurrent laryngeal nerve injuries represent a rate of 1.2 per cent in three hundred and thirty four thyroid operations. An additional 3 patients, 0.9 per cent, sustained temporary nerve injury such as may result from undue traction, crushing or hemorrhage into the nerve area, with demonstrated recovery of function in two to twenty eight weeks. Postoperative hypothyroidism and myxedema were noted in 12 of 288 patients, a rate of 4.2 per cent. This complication is far preferable to persisting toxicity and, in certain thyrocardiac patients, is even desirable. If necessary, it is readily treated.

The long continued use of iodine in the unoperated patient with hyperthyroidism was discouragingly frequent. These patients were more difficult to prepare for surgery, the operative risk was greater, the postoperative reaction was less amenable to control, and a fatal outcome was more frequent. Three patients, or 60 per cent of those who died in the hyperthyroid group, had been given daily iodine for from one to six months before surgery was advised and carried out.

Experience has led us strongly to advise against the use of iodine in these patients until active plans for surgical treatment have been made by the physician and agreed to by the patient. Attempts to control hyperthyroidism with nonsurgical measures not only delay unjustifiably, we believe, ef

fective control of the disease, but increase the likelihood of complications before and after thyroidectomy and thereby lessen the usual safety of the procedure. The iodine-fast patient with hyperthyroidism should disappear as soon as physicians are

ready to accept the facts that surgery is a safe and rapid method for curing hyperthyroidism and that, in outspoken thyroid toxicity, iodine does not produce a cure.

412 Beacon Street

THE PHYSICIAN PREPARES TO ENTER THE ARMY

ROBERT M. ZOLLINGER, M.D.,* AND MARK A. FREEDMAN, M.D.†

BOSTON

THE proposed increase in the size of the Army of the United States indicates that many physicians will find themselves in the armed services in the near future. The average physician is so busy with everyday practice that he has little time to think about the multiple preparations necessary before he enters the service. Many questions arise regarding how to proceed to close the office, provide for dependents and prepare for entrance into the Army. Having experienced these problems and answered many inquiries, we offer the following suggestions. Although many of these suggestions are obvious and others may be outdated or changed radically before this article is published, some of them may be helpful.

CLOSING OFFICE

One should take an inventory of all instruments, equipment and furniture and evaluate these articles in case it becomes necessary to sell them or to collect insurance for fire or theft.

One should arrange for storage of equipment and see that it is fully covered by insurance, unless it is to be used by another physician.

All narcotics should be locked up or returned for credit; it is not necessary to renew the narcotic license.

All case histories, especially cases in which litigation may be involved, should be completed. A physician who is entering the service should instruct his representative or attorney in the use of his files and their contents.

Accounts payable and receivable should be audited and explained in detail to the representative or attorney. A note should be appended to statements rendered for professional services informing patients that one is called to active duty, since this appeal often brings results.

Office subscriptions to popular magazines should be canceled. It is usually wise to continue profes-

sional journals, with a change of address, until one is certain that they are available in hospital libraries of future stations.

Arrangements to cancel or adjust rent or sublet office space should be made. If the renewal of the lease for office space is due in the near future, and there is a possibility of one's being called to active duty, this renewal should contain an army clause to become effective on the date of call to service.

Service for gas, electric light, telephone, laundry and so forth, should be canceled.

Employees should be provided with a letter of recommendation.

Since service in the Army does not release one from the danger of malpractice suits, it is wise to maintain professional protective insurance. However, the validity of such insurance, while one is on duty, especially on foreign soil, should be checked—some companies are issuing a special low-cost policy covering malpractice insurance in military service. The insurance company should be notified of entrance into the service and change of address.

All medical societies of which one is a member should be notified of the date of call to service. Many societies will keep the names of those entering the armed forces on their inactive list until they return, without financial obligation.

It is advisable to take along any instrument, such as an ophthalmoscope or stethoscope, that one has become accustomed to using with ease and without which one may be handicapped.

A request for leave of absence should be written to the secretary of the staff of the hospitals and medical school where appointments are held, or with which one has been affiliated.

It is a matter of personal opinion of how best to notify patients of entrance into the services. This may be done by personal calls, printed announcements or form letters. If one's practice has been assumed by another physician, this fact may also be announced by the above methods.

*Major, United States Army Medical Corps.

†Captain, United States Army Medical Corps.

PROVIDING FOR DEPENDENTS

The chief concern of most physicians will be providing for the family. Budgets must be readjusted to the new fixed income (Table 1). It

are not given a rental allowance. While one is on duty in the United States, allotments of pay can be made only for payment of governmental or commercial life-insurance premiums. On duty out-

TABLE 1. *Approximate Pay of Medical Officers.*

RANK	FIRST LIEUTENANT		CAPTAIN		MAJOR		LIEUTENANT COLONEL	
	MARRIED	SINGLE	MARRIED	SINGLE	MARRIED	SINGLE	MARRIED	SINGLE
Base pay	166.67	166.67	200.00	200.00	250.00	250.00	291.67	291.67
Rental allowance	60.00	40.00	80.00	60.00	100.00	60.00	120.00	80.00
Ration allowance	36.00	18.00	36.00	18.00	54.00	18.00	54.00	18.00
Totals	262.67	224.67	316.00	278.00	404.00	328.00	465.67	389.67

is wise to plan this readjustment early, so that all changes will be gradual and all eventualities may be foreseen.

It is unwise to plan on moving the family until it can be determined when one will be called and where the first permanent station will be located. The first station may be near one's present home. Taking the family is unsatisfactory, since adequate living quarters near army camps are difficult to find, rents are invariably high and there will be frequent and unpredictable changes of station.

It is essential to consult a competent lawyer in planning and settling one's business affairs.

A last will and testament should be made, regardless of dependents.

A power of attorney should be granted the wife or another trustworthy and competent person, so that one's business may be managed properly. A limited power of attorney may be given a secretary, who is familiar with the accounts payable and receivable that will continue for a time after the office is closed.

All documents, such as deeds, wills, insurance policies, copies of power of attorney and birth certificates, should be stored in a safety deposit box accessible to the wife and attorney.*

ARMY PAY AND ALLOTMENT

For the first time, the majority of physicians will receive a relatively fixed salary, varying only with rank, length of service and special compensation for service overseas. This salary, which is paid once a month in cash or by check, may be deposited by the local finance officer in the bank of one's choice. Each officer receives a 5 per cent increase in base salary when he completes three years of active duty, six years of inactive duty or any equivalent combination of service. This is known as a "fogey." A 10 per cent increase in base pay is provided when an officer serves overseas. Single officers, living in adequate quarters provided by the Government,

side the continental limits of the United States or in Alaska, one can allot any or all of the base pay, longevity and ration allowance to any bank or insurance company. These amounts can be calculated from Table 1.

Single officers with dependents may receive married officers' salaries if the dependency is adequately proved by certification and affidavits.

INSURANCE

Since many physicians have major investments in insurance, this subject deserves special consideration.

The validity of all insurance policies while one is in service should be reviewed. Most policies issued during the latter half of 1941 contain a war clause. The clauses that govern the continuation of policies in the event that one is unable to pay the premiums should be clarified. Such problems can be discussed with any competent insurance broker or a qualified representative of the insurance company. There are no set rules for insurance, since each policy is an individual contract, and policies vary with the company and the type of coverage. Although no set directives can be given, the following suggestions may prove of benefit.

A résumé of all insurance policies, listing the name of the insurance company, type of insurance, amount of policy, amount of premium and date on which the premium is due, should be prepared. Copies should be furnished to the persons designated to manage the affairs of the physician who enters the service.

A permanent mailing address (not an army address) should be established in one's name in care of the wife or attorney, so that premium notices will be received and paid promptly.

In general, policies lapse in thirty-one days if the premiums are not paid. A statement of health must be submitted in the following thirty-day period, or policies are finally dropped. Absence without proper safeguards and the impossibility of quick communication invite this danger. If ninety

*LaGarde, R. D. Concerning dependents. *Coast Artillery* 1: 85:14 (Mar-Apr), 1942.

days have elapsed, the policy may then be considered void, and the company may refuse to reinstate the policy on payment of back premiums or may reinstate the policy with a war clause inserted.

It is possible to pay up policies for more than a year in advance by a single cash payment. Interest usually accrues at bank rates, and any excess is refunded if the policy is terminated.

Information should be obtained regarding what happens to each policy if one is unable to pay the premiums from current income.

The better plan is that incorporated in an "automatic premium loan clause." This permits the use of the cash value of the policy for payment of future premiums. If not already included, this clause should be written into the contract. If it is planned to use this method of payment, written authorization must be given to the company. This is not applicable to term insurance, which has no loan value.

If the company will not grant the automatic premium loan option, the policy is governed by the so-called "nonforfeiture option." This option provides the choice of accepting a reduced amount of paid-up or extended insurance at its full value until the cash value of the policy is used up. This selection seems desirable in providing full protection during service in the Army.

Double indemnity is usually not paid in war except for fatal accidents common to civilian life. The disability clause does not hold during military service. Some companies will refund this portion of the premium on a pro-rata basis. Likewise, some companies will reinstate the disability clause after return to civil life if a medical examination is passed.

Is the policy invalidated by airplane travel? If not, is there any limitation concerning the type of carrier and number of flights. In many policies, double indemnity is not paid except in fatal accidents occurring on regular fare-paying passenger lines. Double indemnity would not be paid for accidents occurring in the Army Air Corps.

Term insurance especially must be analyzed. If it is necessary to convert it while one is in service, one should make certain that the war clause is not inserted. One must provide the additional money necessary for conversion back to the date of purchase, to avoid insertion of the war clause. If term insurance is converted gradually, the dates of conversion and amount of increase of premium must be carefully explained to those responsible for paying the insurance premium. An immediate conversion to ordinary life insurance is advisable if financially possible.

To avoid nonpayment of premium, it is possible, if on duty outside continental United States or in Alaska, to have the Government pay premiums directly to the insurance company and make the necessary deduction from base pay. This is called "payment by allotment." It will be necessary to adjust the premium to a monthly payment plan, for annual and quarterly payments are not possible by allotment.

Government insurance is available up to \$10,000. This cheap and highly desirable insurance may be obtained by consultation with the adjutant of the organization. It is not available until after induction into the service. Although it is initially term insurance, it may be converted after a year and before five years have elapsed. The monthly premiums vary from \$7.10 at thirty years of age to \$8.50 at forty.

The advisability of continuing health and accident insurance policies should be considered, since the benefits from these policies are limited while the physician is in the armed services. Most policies are good only for conditions common to civilian life in the United States. Noncancelable policies merit special consideration, for they may be impossible to obtain when one returns to civilian life.

All other types of insurance should be renewed, and one should be certain that coverage is complete for fire, theft, liability and so forth on car, household goods and real estate. Adequate preparation for payment of such premiums, many of which fall due every three years, should be made.

All policies should be stored in a safety deposit box.

It is wise to provide the wife or attorney with a copy of marriage certificate and birth certificates of oneself, wife and dependents so that relationship may easily be proved if it becomes necessary to collect pensions or insurance. These documents should be placed in a safety deposit box.

TAXES AND MORTGAGES

Service in the Army does not excuse one from payment of taxes. Although the Soldiers and Sailors Civil Relief Act of 1940 permits deferment of payment of federal taxes by members of the armed forces, this deferment is not automatic. Inability to pay taxes from current income must be proved by the submission of a sworn statement of financial condition at the time the tax return is filed. The attorney should be provided with a list of taxes payable and the dates on which they are due, and with all information necessary to file income-tax returns on income from practice and investments. Arrangements should be made for

payment or readjustment of any mortgages that may be held. Army salaries are subject to the state and federal income taxes.

Although the Relief Act of 1940 provides protection for men in the service on certain other classes of debt in and prior to the passage of the act, one should consult a competent attorney in any specific case in which relief is desired.

UNIFORM

It is customary to report for active duty in uniform. It is, of course, a great temptation to buy an extensive wardrobe. It cannot be overemphasized that one should purchase only a minimum of clothing. Great savings and better selection can be effected if one purchases most articles from the post exchange and quartermaster after reporting for duty.

The prescribed uniform varies with the type of assignment and with the climate. A safe minimum purchase providing a standard dress uniform regardless of the location of station or time of year is as follows:

- 1 overseas cap.
- 1 woolen blouse with cloth belt (Sam Browne belts are no longer required).
- 1 pair of woolen trousers (either 'pink' or to match blouse).
- 1 cotton shirt
- 1 woolen shirt (field).
- 1 web belt (plain buckle).
- 2 pairs of solid color tan or brown socks.
- White or tan handkerchiefs
- 1 necktie of new M-3 shade (black ties are no longer worn).
- 1 overcoat (if possible, one should not buy an overcoat until arrival at post; if weather is inclement, a gabardine raincoat may be worn)
- 1 complete set of insignia (one should refer to *Officer's Guide* for correct placement on uniform).

All solid tan and brown shoes are acceptable.

(It is not considered necessary to wear any special military shoe unless one is ordered to do so. One should remember that there is much walking and marching during the initial period of training on active duty, and should provide oneself with a pair of comfortable, waterproof, well broken in high shoes.)

Every article of clothing should be marked with one's name. Rank and name of organization should be omitted. Linen or rayon tape, embroidered or stenciled with indelible ink, is most frequently used. A timesaving device is a rubber name stamp with an indelible ink pad for stenciling flat pieces, such as handkerchiefs, sheets and towels.

All personal effects should be stored, and all woolen clothing should be cleaned and made mothproof before storage.

Useful reference books that may be purchased are *Officer's Guide* (seventh edition—February, 1942), *Military Medical Manual* and *Handbook of the Medical Soldier*.

The following luxuries will add much to one's comfort and enjoyment during camp life but are not essential: radio, camera, electric razor, spot-type bed lamp, small bedside floor rug and so forth.

The change from civilian to army life is radical, and yet the readjustment is rapid, and many a busy physician will appreciate the change. Incidentally, he may be called on to assume the responsibility of doing his own laundry. If so, all woolens should be treated with due respect and washed carefully in lukewarm water. Many a new officer has been horrified by the atrophy of his beautiful hand knit socks following his first effort at the wash tub.

days have elapsed, the policy may then be considered void, and the company may refuse to reinstate the policy on payment of back premiums or may reinstate the policy with a war clause inserted.

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- 1 cotton shirt
- 1 woolen shirt (field)
- 1 web belt (plain buckle)
- 2 pairs of solid color tan or brown socks
- White or tan handkerchiefs
- 1 necktie of new M-3 shade (black ties are no longer worn).
- 1 overcoat (if possible, one should not buy an overcoat until arrival at post, if weather is inclement, a gabardine raincoat may be worn)
- 1 complete set of insignia (one should refer to *Officer's Guide* for correct placement on uniform).

All solid tan and brown shoes are acceptable. (It is not considered necessary to wear any special military shoe unless one is ordered to do so. One should remember that there is much walking and marching during the initial period of training on active duty, and should provide oneself with a pair of comfortable, waterproof, well broken-in high shoes.)

Every article of clothing should be marked with one's name. Rank and name of organization should be omitted. Linen or rayon tape, embroidered or stenciled with indelible ink, is most frequently used. A timesaving device is a rubber name stamp with an indelible ink pad for stenciling flat pieces, such as handkerchiefs, sheets and towels.

All personal effects should be stored, and all woolen clothing should be cleaned and made moth proof before storage.

Useful reference books that may be purchased are *Officer's Guide* (seventh edition—February, 1942), *Military Medical Manual* and *Handbook of the Medical Soldier*.

The following luxuries will add much to one's comfort and enjoyment during camp life but are not essential: radio, camera, electric razor, spot type bed lamp, small bedside floor rug and so forth.

The change from civilian to army life is radical, and yet the readjustment is rapid, and many a busy physician will appreciate the change. Incidentally, he may be called on to assume the responsibility of doing his own laundry. If so, all woolens should be treated with due respect and washed carefully in lukewarm water. Many a new officer has been horrified by the atrophy of his beautiful hand knit socks following his first effort at the wash tub.

EXPERIMENTAL APPLICATION OF SULFONAMIDE DRUGS TO THE CEREBRAL CORTEX*

FRANC D. INGRAHAM, M.D.,† AND EBEN ALEXANDER, JR., M.D.‡

BOSTON

BECAUSE of war conditions, widespread use of the sulfonamide drugs in wounds of all parts of the body has developed. The obvious effectiveness of these chemicals in helping to minimize infections¹ has resulted in their clinical employment with very little experimental basis, whereas ordinarily there would be ample opportunity for

wise made available to the interested medical public. Several extensive projects are now under way, and it is probably just as well that these be made by several observers, since important discrepancies in results have already been reported. Pilcher and his associates,² who are carrying on an investigation of the chemotherapy of intracranial infections,

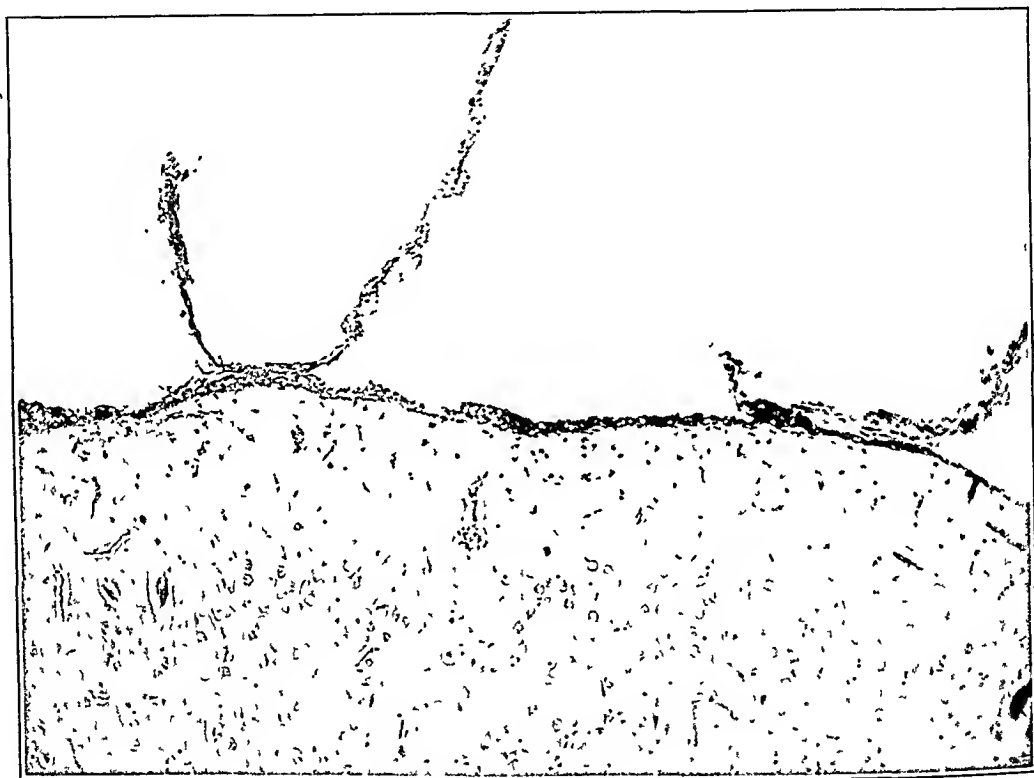


FIGURE 1. Cat No. 1.

Photograph of a section of the cortex of a cat in which operation had been performed under nonsterile conditions but with sulfamilamide added ($\times 125$).

thorough laboratory trial. This has been particularly true in craniocerebral injuries, in which the opportunity for clinical trial has been all too readily available.

It is apparent that experimental control of this type of chemotherapy,—that is, direct application to the brain and meninges,—is being undertaken in many laboratories, and some surgeons have had an opportunity to see even late effects of such application in patients. To date, extraordinarily little accurate information has been published or other-

were so impressed by the harmful effects of the use of sulfathiazole that they published a preliminary report on the convulsions produced by intracranial implantation of sulfathiazole. Almost concurrently with their report, Penfield,³ following a trip to Great Britain, refers to the fact that some British neurosurgeons have been so favorably impressed by the effect of local application of sulfathiazole that they have taken to placing it routinely within all craniotomy incisions before closure. It seems obvious that the experimental phase of this problem lags considerably behind the clinical. Probably the most complete and most valuable work reported so far, from the Montreal Neurological Institute, was summarized recently by Hurteau.⁴

*From the Department of Surgery of the Children's Hospital and the Harvard Medical School.

†Neurosurgeon, Children's Hospital, associate in neurosurgery, Peter Bent Brigham Hospital, associate in surgery, Harvard Medical School.

‡Assistant in surgery, Harvard Medical School.

Undoubtedly, other complete studies will be reported in the near future.

In the hope that some unnecessary duplication of effort may be avoided, these somewhat simpler preliminary experiments are recorded. Sulfanilamide, sulfathiazole and sulfadiazine were applied to the cortex of cats under sterile and unsterile conditions, and since we were most interested in the use of sulfadiazine, this drug was applied to the surface of the brains of three monkeys.

The cat experiments were carried out as follows. With full aseptic surgical technique, a midline incision was made, the temporal muscles incised, and a trephine opening 1.5 cm in diameter made in

repeated, the animal was sacrificed at the end of twenty-nine days, and a mild inflammatory reaction was found.

It is interesting that, except for the control

TABLE 1 Summary of Cat Experiments

CAT No	DRUG USED	POST-OPERATIVE DAY KILLED	FINDINGS ON TRAUMATIZED SIDE	FINDINGS ON NONTRAUMATIZED SIDE
Operation performed under sterile conditions				
86	None	14	Normal	Normal
87	Sulfanilamide	36	Normal	Normal
84	Sulfathiazole	7	Normal	Normal
70	Sulfathiazole	29	Mild inflammation	Mild inflammation
25	Sulfadiazine	23	Normal	Normal
Operation performed under nonsterile conditions				
89	None	5	Severe meningoencephalitis	Severe meningoencephalitis
1	Sulfanilamide	19	Dura adherent	Dura adherent
2	Sulfathiazole	14	Normal	Normal
3	Sulfadiazine	26	Normal	Normal

the parietal bone on both sides. The dura was opened on both sides, and on one side, the pia arachnoid was torn and the cortex was traumatized very superficially with a sharp needle. In the control animal, no drug was used. The sulfonamide drugs, in powder form, were applied to the cortex of both sides and to the superficial tissues. Five tenths of a gram of powder was used in each case, a definite layer completely covering the exposed brain being obtained. In a second group of animals, the same operation was then carried out, and drugs were applied under nonsterile conditions; the instruments used were clean but not sterilized, the animals were not shaved, and no cleansing agent was applied to the skin. The results of these experiments are shown most clearly in Table 1 and Figures 1 and 2.

In general, there was surprisingly little reaction to the drugs. One cat in which sulfathiazole was used died seven days after operation, and the cause of death was not clear. Other investigators⁵ have reported that animals in which sulfathiazole was used have had convulsions and have died, presumably because of local irritation and absorption of the drug. In the animal in our experiment, no convulsions were observed, and the survival time seems long for death to have been due to absorption of the drug. When the experiment was



FIGURE 2 Cat No. 89

Photograph of a section of the cortex of a cat in which operation had been performed under nonsterile conditions and without a sulfonamide drug added ($\times 125$).

animal that developed a severe meningoencephalitis, the cats subjected to operation under nonsterile conditions did extremely well. There was a slight

TABLE 2 Summary of Monkey Experiments

MONKEY No	DOVE FLAP	DRUG USED	POST-OPERATIVE DAY KILLED	FINDINGS
1	Not replaced	Sulfadiazine	54	Adhesions of muscle dura and cortex
2	Replaced	Sulfadiazine	45	Inflammatory reaction in dura
3	Replaced	Sulfadiazine	45	Normal

inflammatory response to the drugs, but no actual infection, and when sulfadiazine was used there was no perceptible inflammation.

Since sulfadiazine is probably the most effective of the three drugs in inhibiting the growth of a variety of organisms that would be likely to contaminate war wounds, we were most interested in its application to the cortices of three monkeys (*Macacus rhesus*). A bon

turned down under sterile conditions, the dura opened widely, and 0.5 gm. of sulfadiazine powder

fifty-four days. In the second experiment, there was a mild inflammatory reaction in the dura, and



FIGURE 3. Monkey No. 1.

This monkey was operated on with sterile precautions, the bone flap not being replaced; sulfadiazine was added. The upper photograph shows the gross appearance of the brain, before and after removal of the dura; the temporal muscle was adherent at the site of the flap. The lower photograph shows a section of the cerebral cortex at the site of the adhesion ($\times 125$).

spread over the cortex, dura, bone and superficial tissues. The experiments are summarized in Table 2. In one experiment, the bone flap was not replaced, and dense adhesions between muscle, dura and cortex resulted, as shown in Figure 3, taken when the animal was sacrificed at the end of

a collection of the powder was still grossly visible under the bone flap after forty-five days (Fig. 4). In this and the third experiment the dura stripped away from the arachnoid without any adhesions, and no drug was visible on the surface of the brain.

Unfortunately, these monkeys were extremely difficult to handle, and it was possible to make only a few observations. There was remarkably little inflammatory reaction except in the control cat under nonsterile conditions.

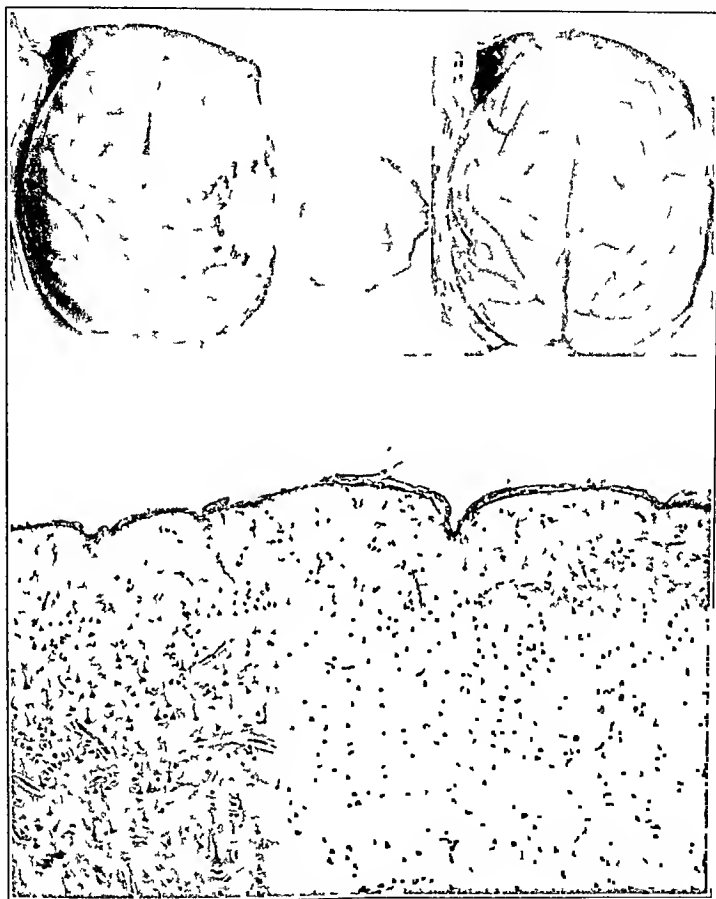


FIGURE 4 Monkey No 2

This monkey was operated on with sterile precautions sulfadiazine was added and the bone flap replaced. The upper photograph shows the gross appearance of the brain before and after removal of the dura and the inner surface of the bone flap where some of the drug still remained. The lower photograph shows a section of the cerebral cortex ($\times 125$).

postoperative blood and spinal fluid determinations in only one. On this occasion, twenty-four hours postoperatively, the blood sulfadiazine level was 17 mg per 100 cc, and the spinal fluid level 10 mg per 100 cc.

SUMMARY

Sulfanilamide, sulfathiazole, and sulfadiazine were applied directly to the cerebral cortex of 7 cats under sterile and nonsterile conditions. There

Sulfadiazine was applied to the cerebral cortex of 3 monkeys. There was no perceptible inflammatory reaction, except in one, in which the bone flap was left out.

One may conclude that sulfadiazine powder, which is generally agreed to have a bacteriostatic action on the widest variety of organisms, can be safely used in the presence of gross contamination when the brain is not severely damaged. Further

work must be done to determine whether or not this conclusion can be applied to more complex craniocerebral injuries.

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MEDICAL PROGRESS

VIRUS PNEUMONIAS. II. PRIMARY ATYPICAL PNEUMONIAS OF UNKNOWN ETIOLOGY*

JOHN H. DINGLE, M.D.,† AND MAXWELL FINLAND, M.D.‡

BOSTON

DURING the last few years, there has been a great deal of interest in the increasing numbers of cases of acute respiratory infection associated with atypical pulmonary lesions in which the common pathogenic bacteria do not seem to play an etiologic role. The vast majority of the reported cases have occurred in adolescents and in young adults. Many of the reports have come from schools,¹⁻⁴ colleges⁵⁻¹⁰ and army camps.^{11, 12} Hospital personnel, particularly interns and nurses, have also featured prominently among the reported cases.¹³⁻¹⁶ Although the mortality in these cases has been extremely low, the period of disability has been quite long. With the accelerated program of studies now in effect in most universities and with the rapid increase in the size of the Army, accompanied as it is by a shorter training period, these cases may constitute a significant problem from the point of view of "time out" from studies or the loss of man-days from training.

The name "virus pneumonia"¹⁷⁻²² has been applied rather loosely to this group of cases and is probably the one most widely employed by practitioners. In most cases, the only justification for the use of this term is the failure to obtain pathogenic bacteria that can be considered etiologic. Individual authors have justified their use of the term on the basis of suggestive histologic findings in the pulmonary lesions,^{17, 20, 22} or on the

results of studies that suggested the presence of filterable agents.¹⁴ Numerous other designations have been used in the description of similar cases. They include "acute influenzal pneumonia"¹¹; "acute pneumonitis"^{2, 3, 12}; "pneumonitis"^{23, 24}; "acute interstitial pneumonitis"⁷; "atypical pneumonia with leukopenia"⁸; "current bronchopneumonia of unusual character and undetermined etiology"¹⁵; "bronchopneumonia of unknown etiology, Variety X"¹⁶; and "atypical bronchopneumonia of unknown etiology."¹⁴ Most authors have believed that they were dealing with a specific infectious disease that constitutes a new entity.^{7, 13} Reimann¹³ suggested that it be called "acute infection of the respiratory tract, Type A" or perhaps "Type A virus pneumonia" if the virus etiology is confirmed,¹³ or that the more general term "grip"¹⁴ be used. Scadding²⁵ has attempted to classify certain more limited groups of cases according to the character of the pulmonary lesion, particularly according to their distinctive roentgenographic shadows, and has applied the name "disseminated focal pneumonia" to some of them; others he²⁶ called "benign circumscribed pneumonia." In a recent "official statement" to the Surgeon General of the Army prepared by the director of the Commission on Pneumonia, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the United States Army, it was suggested that, for purposes of classification, these cases be separated from other pneumonias and designated "primary atypical pneumonia, etiology unknown."²⁷

This paper considers the clinical aspects of such cases and the results of attempts to establish the etiologic agent. A review of the cases of pneu-

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual*, Vol. III, 1942 (Springfield, Illinois: Charles C Thomas Company, 1942. \$5 00).

*From the Thorndike Memorial Laboratory, Second and Fourth (Harvard) Medical Services, Boston City Hospital, and the Department of Medicine and the Department of Bacteriology and Immunology, Harvard Medical School.

†Associate in medicine and instructor in bacteriology and immunology, Harvard Medical School, assistant physician, Thorndike Memorial Laboratory, Boston City Hospital.

‡Assistant professor of medicine, Harvard Medical School; associate physician, Thorndike Memorial Laboratory, and chief, Fourth (Harvard) Medical Service, Boston City Hospital.

monia due to known viruses and rickettsias was given in the first section of this report.^{28*}

Primary atypical pneumonia of unknown etiology is, in all probability, not a single disease but a syndrome that may be produced by a number of agents.²⁷ Nor is it a new pathologic syndrome, in spite of the numerous recent reports and the apparent increase in incidence. Positive identification of cases of atypical pneumonia, as reported in the literature, is difficult because no single criterion—clinical or laboratory—characterizes the syndrome. Moreover, clinical criteria for the diagnosis of such related infections as grippe, influenza and bronchopneumonia, which may simulate this disease, vary widely. Despite these difficulties, the entire syndrome can usually be differentiated from similar conditions of known etiology. On this basis, it is apparent that the pneumonia was seen clinically as long ago as 1872,^{29, 30} and a similar pathologic picture was described at about the same time.^{31, 32} With the introduction and use of roentgenography of the chest, further reports appeared, particularly in the literature dealing with tuberculosis and influenza. It seems likely that the disease was prevalent before the pandemic of influenza in 1918 and that it existed in the military forces, where it was given such names as "catarrhal fever" and "soldier's pneumonia."³³⁻⁴² In addition, almost all the reported cases of pneumonia have included a group for which the etiology either could not be determined or was thought to be one of the "higher types" of pneumococci. Clinically, many of these patients did not have typical pneumococcal pneumonia, the course of illness was unaffected by specific therapy, and the outcome was ordinarily complete recovery. Some, if not most, of these patients probably had atypical pneumonia.

Since the papers of Gallagher¹ and Bowen,¹¹ this type of illness has been more carefully differentiated, and cases occurring both sporadically and in small outbreaks have been reported under the variety of names listed above. Recent developments in the knowledge of viruses affecting the respiratory tract have established a preliminary basis for segregation of some of these cases etiologically, but the cause of a large number still remains unknown.

Thus, it is apparent that the characterization of atypical pneumonia is difficult and confusing, and will remain so until the etiologic problem is solved. Diagnosis can now be made only by clinical and radiologic criteria—no one of which is specific—or by exclusion. A description of the character-

istics of the morbid process can only be as reliable as the diagnosis, which likewise is the basic limiting factor in the evaluation of experimental investigation. For simplicity in discussion, primary atypical pneumonia of unknown etiology will be referred to as a disease, although at present it must more accurately be considered a syndrome, possibly with multiple etiologies.

EPIDEMIOLOGY

Occurrence. The full extent of the distribution of atypical pneumonia is not known. Its occurrence has been noted in all parts of the United States,^{1, 3, 6-10, 12-10, 18, 43} in Honolulu,¹¹ in England²³⁻²⁶ and probably on the continent of Europe.³⁹ These reports suggest a widespread distribution, which probably lacks confirmation only because of limited recognition. Rates of attack cannot be determined satisfactorily from the data available in the literature. The disease apparently exists sporadically and in small outbreaks.^{15, 44} Bowen's¹¹ figures indicate a yearly attack rate varying from less than 1 to approximately 6 per 1000 in white troops during a three-year period in Honolulu. The incidence rate at Cornell University was approximately 9 per 1000 for the academic year 1937-1938.⁷ Reimann¹³ observed 25 cases among a hospital staff composed of 813 persons. Daniels⁴ reported 13 cases in a school of about 90 girls during a six-week period—an incidence of almost 15 per cent. Cases of atypical pneumonia have comprised from less than 1 to about 6 per cent of the total admissions for respiratory diseases at different infirmaries and hospitals.^{5, 10-14} It seems likely that the yearly increase in cases recently noted at several clinics may be due, in part at least, to more frequent recognition. It is possible, however, that these are epidemic forms of the disease.

Age and sex. The age distribution in the reported outbreaks has thus far been almost entirely limited to adolescents and young adults. Most of these outbreaks were observed in schools or military posts, where the age of the personnel is limited. The majority of the patients seen in civilian hospitals, however, have been young adults, although the span of age has varied from four to eighty years.^{1-3, 12-10, 23} The limited age distribution may therefore be of significance, although recognition and opportunity for spread may be major factors. Adams^{20, 22} has recently described in infants a somewhat similar virus pneumonia to which adults were apparently not susceptible. This disease, which differs in certain respects from the atypical pneumonias under discussion, is considered below. There is no rec-

*Our attention has been called to the recent report of 2 fatal cases of lymphatic choriomeningitis with pulmonary involvement by Smadel et al.⁴⁵ who isolated this virus from the lungs and other tissues in both cases.

ognized difference between the sexes so far as susceptibility or immunity is concerned.

Season. The seasonal distribution is variable, and sporadic cases apparently occur regardless of season.^{9, 13-16} Many of the reported outbreaks have occurred in the late fall and winter,^{3, 7, 9, 15} although the epidemic described by Reimann and Havens¹⁴ took place between January and May, with the peak of incidence in February. Murray⁹ pointed out that the majority of his cases occurred in November and December, whereas the greatest incidence of the other upper respiratory infections was noted in February and March. McKinlay and Cowan¹⁰ also noted that an increase in upper respiratory infections did not call forth a corresponding increase in atypical pneumonia. These observations, perhaps, tend to dissociate atypical pneumonia from the common cold and other minor respiratory infections.

Spread. Little is known regarding the mode and manner of spread of atypical pneumonia. The general consensus is that it is transmitted by contact but is not highly communicable.^{3, 9, 15, 16} Multiple cases have been seen in members of the same family or of the same household who have had opportunities for close contact.^{4, 7, 13} Smiley and his co-workers⁷ noted that the infectiousness of the disease was apparently not great in the absence of cough. The high incidence of infection in nurses and doctors^{8, 15, 16} supports the theory of contact spread and also suggests that prolonged contact with patients may be necessary. One interpretation may be that the general resistance to atypical pneumonia is high, and as a result a large dose of the infecting agent is necessary to produce the disease. Or the infection may be more widespread than is now generally suspected, many of those afflicted presenting the symptoms and signs of a mild systemic and respiratory disease without demonstrable pulmonary lesions. Those receiving a larger primary inoculum through close contact may be likelier to develop pneumonia. The concept of mild and even inapparent or carrier infections is of considerable interest clinically and epidemiologically because of the necessity of delimiting this disease as a specific entity. A satisfactory laboratory test based on etiology will have to be obtained before this can be accomplished.

Reimann¹³ noted that in a group of 5 patients who had familial contact there were 2 cases of severe infection and 3 of mild disease. In an epidemic among 813 persons at the Jefferson Hospital, he and Havens¹⁴ described 407 cases of respiratory disease. The majority of these were mild infections, and the patients remained ambulatory. A clinical and roentgenologic diagnosis of

acute tracheobronchitis was made in 6 per cent and of pneumonia in 6 per cent. These investigators believed that the patients were ill presumably of the same disease, and further stated, "Cases of the mild form far outnumbered those of the severe form, and for this reason we believe it to be misleading to apply restrictive names indicating special forms of bronchiolitis or pneumonia to cases of the severe form alone, as many have done." Gallagher² also noted 11 cases of mild infection, without pulmonary involvement, that epidemiologically both preceded and followed definite cases with so-called "pneumonitis." Longcope²¹ has observed that patients may apparently contract a severe form of infection from those who have had a mild attack, or that the reverse may occur. It seems likely that such cases as these must be taken into consideration when one is attempting to elucidate the nature and manner of spread of atypical pneumonia.

Incubation period. Reliable data regarding the incubation period of atypical pneumonia are likewise lacking. Reimann and Havens¹⁴ believed that it might be as short as one or two days, but other investigators have estimated the period to be between seven and twenty-one days, or even longer.^{3, 4, 7, 9, 15, 16}

CLINICAL ASPECTS

A clinical description of atypical pneumonia at present must be almost entirely restricted to cases presenting clinical or roentgenologic signs of pulmonary involvement. In spite of the great likelihood that related nonpneumonic or inapparent forms of infection occur, there are no reliable means by which such cases can be differentiated from other minor upper respiratory illnesses. Even in the group showing pulmonary involvement diagnosis may not be easy. From the reports in the literature, it is difficult to accept certain cases as being consistent with atypical pneumonia, although it is entirely possible that the written descriptions convey an impression contrary to that which would be obtained on actual examination of the patient. An attempt is therefore made to present the generally accepted picture of atypical pneumonia; the significant variations that have been reported are noted.

Onset. The onset in the majority of cases is gradual and insidious over a period varying from one day to a week or more. Kneeland and Smetana¹⁵ described the onset as "grippelike." Preceding or accompanying upper respiratory infections have been noted in from 50 to 75 per cent of the cases in some outbreaks,^{2, 3, 9, 10} whereas in others catarrhal symptoms have been rare^{13, 14} and "influenzalike" symptoms absent.

The onset has been described as sudden or abrupt by Daniels⁴ in all his cases, and by Murray⁹ in about one fourth of his cases. It is rarely so abrupt and dramatic as that in pneumococcal pneumonia.

Symptoms. The presenting symptoms are ordinarily quite uniform early in the disease, regardless of the subsequent severity and course of the illness. Fever, cough, malaise, headache and chilliness are almost constant complaints. The temperature may be at any level between 99 and 105°F., or more, but is usually between 100 and 103°F. Cough, at this stage, is very distressing to the patient. It is dry and may occur in paroxysms, which are difficult to control. Substernal pain or soreness and tenderness of the abdominal muscles frequently result from tracheal irritation and cough. The cough may be productive, however, at the onset or early in the course.^{9, 16} The sputum is mucopurulent and may be blood streaked, but is not rusty or suggestive of prune juice. Malaise, aches and pains, and prostration may be out of proportion to the general appearance of the patient. Headache is often severe and is frequently frontal or periorbital, but may be general or localized anywhere. Sensations of chilliness and shivering usually alternate with periods of feverishness, but shaking chills and rigor seldom occur. The throat may be dry or sore before or at the time of onset, but usually sore throat does not persist beyond the first few days of illness. Drenching sweats occur in some cases.^{7, 9, 13, 14} Gastrointestinal symptoms are usually not a feature. Other symptoms, such as stiff neck, vertigo, abdominal distention, dyspnea, cyanosis and mental confusion and disorientation, occur rarely or are seen later in the course of the disease.

Physical signs. Physical examination early in the disease usually reveals little that is abnormal. Fever is almost constantly present, but the majority of the patients do not appear to be so ill as their fever or subjective complaints would warrant. Some patients appear moderately or severely ill, with evident prostration and, occasionally, dyspnea and cyanosis. Aside from pharyngeal injection and, rarely, a palpable spleen,⁹ the examination is negative. The pulse rate ordinarily is within normal limits or low. Respirations are usually normal. Pulmonary signs, if present, are generally limited to fine or medium moist rales occurring late in inspiration.

Laboratory findings. The white-cell count is normal in almost all cases early in the disease. Both leukopenia and leukocytosis are infrequent in the absence of other contributing causes. The sedimentation rate may be elevated, but other laboratory tests are usually negative.

X-ray findings. The first evidence of pulmonary involvement is usually obtained by roentgenologic examination of the chest. Lesions may be apparent on admission and are almost always found within the first few days of the disease. The character, size and location of the lesion are variable.^{4, 9, 11, 13, 16, 21, 26, 47, 48} In the majority of patients, the first change noted is an increase in the size of one or both hilar shadows, followed by an infiltration, which extends outward from the hilum toward the periphery of the lung fields, often in the shape of a fan or wedge, and fades out gradually into the normal lung parenchyma. Origin of the lesion at the periphery of the lung has not been described in typical cases. Most frequently, the lesion is found in one of the lower lobes, but it may occur anywhere. Bilateral involvement is not uncommon, and is found in 20 per cent or more of the cases.⁸ The process may spread to the adjoining lobes and, infrequently, is very extensive, involving all, or almost all, the lobes. Usually, the infiltration is soft, either mottled or homogeneous, and denser near the hilum. It is rarely so dense and circumscribed as that in pneumococcal pneumonia, and seldom does it occupy more than a portion of a lobe.

A number of variations in the radiologic picture have been noted, which may be striking. A fairly well-localized, but not sharply defined, lesion may be found in the lower lobes, particularly in one or the other cardiophrenic angle. The process may be light, diffuse and mottled in any portion of the lung field. There may be multiple small areas of soft infiltration that increase in size and become irregularly confluent; or there may be areas of diffuse, rather coarse mottling in foci varying from 2 to 5 mm. in diameter—the “disseminated focal pneumonia” of Scadding,²⁵ which may be impossible to distinguish from tuberculosis. Kornblum and Reimann⁴⁵ have described the picture of “acute tracheobronchitis,” which they believe represents the same infectious process, as a bilateral increase in the hilar and trunk shadows, with indistinct outlines, soft mottling about the hilum and generally hazy lung fields. Similar findings have been noted in influenza.⁴⁷

Resolution of the process is usually slow, but the shadows may at times be quite transitory.^{26, 46} The process often clears from the periphery of the lesion, which becomes more mottled and then fades. Increase in the size of the hilar shadows may persist for several weeks.

Thus, the radiographic picture, although fairly characteristic, may show sufficient variations to be confused with that of pneumococcal pneumonia, bronchopneumonia, acute bronchitis, tuberculosis, pulmonary abscess, acute bronchiectasis, metastatic

infiltration and, of course, the known virus and rickettsial diseases that involve the lung.²⁵

Course. The course of the disease is generally mild, although cases of varying severity and even fatal ones have been reported.^{13, 15, 16} Therefore, the course will be described separately for mild, moderately severe and severe types; one should bear in mind that the differences are chiefly of degree and not of kind.

Patients suffering from the *mild form* of illness usually show the maximum rise in temperature within three days after onset. The temperature may vary from 99 to 105°F.; it may be sustained but is frequently swinging. Defervescence is usually slow, by lysis, for the next few days. The average febrile period is seven or eight days, although it varies considerably. Allen,¹² for example, reported that 68 per cent of his cases had fever for three to eleven days, whereas 12 per cent were febrile for more than twenty days. Headache and chilliness usually persist throughout the febrile period, and the cough ordinarily becomes productive as the disease progresses. Cyanosis and dyspnea are rare. Malaise, lassitude and fatigue often persist several days or weeks after the acute stage of the illness, whereas sore throat is usually present for only the first few days. Unusual sweating has been noted in certain of the outbreaks.^{9, 13} Bradycardia is common, and the respiratory rate is frequently normal or only slightly elevated.

Physical signs are frequently limited to rales over the involved area, often appearing after three or four days of illness or even longer. In most cases, the rales are fine or medium moist and sticky, and occur late in inspiration, although in some cases they have been described as coarse and explosive.¹⁶ During the later stages, when the cough becomes productive, coarse, wet rales and rhonchi may be present. Dullness may be noted, but it is often slight and little more than an increased sense of resistance. Abnormal breath sounds, increased tactile fremitus and the other signs of consolidation are infrequent, but may be found in from 13 to 15 per cent of the cases.^{2, 3, 9} Spread of the lesion may be detected by physical or radiologic examination and may be associated with exacerbation of symptoms and fever. Other abnormal physical findings are not frequent. Splenomegaly has been noted in a few cases⁹; abdominal distention is unusual. Herpes and pleural effusion are rare.^{9, 15} The ordinary laboratory tests give results within normal limits throughout the course. Ordinarily, the physical signs and objective evidences of illness are gone within two or three weeks after onset, but complete subjective recovery may not occur for four to six weeks.

Complications are not commonly observed, but those described are pharyngitis, tonsillitis, sinusitis, otitis media, pneumonia and empyema due to the

hemolytic streptococcus,¹⁰ urticaria, ulcerations on the palate and persistent productive cough suggesting bronchiectasis.

The *moderately severe cases* differ in no significant particulars from the mild cases, except that the patients feel and look sicker. The progress of the disease may be more rapid. Cough and headache may be more pronounced. Dyspnea and cyanosis may be present. The temperature may persist longer and at a higher level, and may be associated with tachycardia and an increased respiratory rate. Spread of the lesion and relapses may occur. There may be little or no correlation between the clinical severity of the infection and the extent of pulmonary involvement by x-ray or physical examination. Not infrequently, the total white-cell count becomes elevated as the disease progresses, without any apparent evidence of secondary bacterial invasion. Complications may be somewhat more frequent, but are of the same type in these cases as in the mild ones.

In the *severe form*,^{14-16, 21} patients usually have an onset of infection that is similar to that described for the mild cases. The symptoms are more pronounced, however, and the progress of the disease to a severe state may be rapid. Fever, severe headache and persistent cough are the outstanding features. Prostration is marked. Dyspnea and cyanosis are usually present in these cases, and the breathing may be rapid, obstructive and asthmatic. Epistaxis, chills and sweating may occur. Drowsiness, meningismus and coma have been described. The temperature may remain elevated, as in typhoid fever, or may be swinging or "septic." Relapses, giving a biphasic or saddle-back temperature curve, are not uncommon. The pulse may be relatively slow, but more frequently it is rapid and more in proportion to the fever than in the milder cases.

Examination of the chest physically and roentgenologically reveals involvement of variable extent that frequently spreads over a considerable portion of the lung fields. Moist rales and rhonchi are the outstanding features, however, and evidence of dense consolidation is not the rule. Other associated findings are polyarthritides, erythematous rash, pleural effusion, thrombophlebitis, evidence of myocardial involvement and signs of involvement of the central nervous system. These findings are rare, however, and, as mentioned above, it is difficult to be certain that they are related to the same process in the absence of specific diagnostic criteria based on etiology.

Laboratory studies in these severe cases may show a moderate secondary anemia and a gradual elevation of the white-cell count as the disease progresses. The urine may show albumin in proportion to the fever. The sedimentation rate is

elevated.¹⁵ In a few cases, liver damage has been suspected on the basis of slight jaundice, reversal of the albumin-globulin ratio, bromsulfalein retention and a shifting Wassermann reaction.¹⁵

The duration of the acute illness is usually two or three weeks, but it may be six to eight weeks or even longer before complete recovery has occurred and the chest is clear by physical and x-ray examination. Although complete recovery is usual, death may result from the disease itself, from secondary bacterial invasion or from the infection superimposed on pre-existing organic disease. McKinlay and Cowan¹⁰ observed a fatal case complicated by pneumonia and empyema due to the hemolytic streptococcus. In a series of 40 cases described by Longcope,^{16, 21} there were 3 fatal cases, 2 of which were in patients with chronic rheumatic heart disease with mitral stenosis and insufficiency.

Atypical Pneumonia in Infants and Children

Although the outbreaks of atypical pneumonia described in the literature have been almost entirely limited to adolescents and young adults, it seems probable that the disease is not confined to this age group. Several investigators^{12, 23, 26, 46} have described apparently identical illnesses in children between the ages of four and nine years. Recently, Adams, Grier, Evans and Beach^{20, 22} have described two epidemics of respiratory disease in young infants up to thirty-two weeks of age. Low-grade fever, cough, dyspnea and cyanosis were the outstanding features. The only characteristic signs in the chest were widely scattered fine rales. Radiologic examination revealed a patchy infiltration, particularly in the upper lobes. Resolution of the process was slow. The average case fatality rate was 20 per cent, but the rate was especially high in those infants who had been born prematurely (82 per cent). Somewhat similar types of illness have been described previously, usually following measles, pertussis or other conditions.^{17, 18, 49}

PATHOLOGY

Knowledge of the pathology of atypical pneumonia is limited because of the low mortality of the infection. The chief pathological features of the fatal cases reported by Kneeland and Smetana¹⁵ and by Longcope^{16, 21} are those of a patchy, hemorrhagic, interstitial bronchopneumonia associated with acute bronchitis and bronchiolitis. Grossly, there are areas of atelectasis and emphysema, small areas of red or gray consolidation, which in some places have apparently become confluent, and reddened bronchi filled with mucoid or purulent exudate. Microscopically, the alveolar exudate may be hemorrhagic or mononuclear in

some areas, whereas in others there is evidence of organization. The alveolar septums may be infiltrated with mononuclear cells and may later show thickening, with a decrease in the size of the alveolar spaces. The process may be most marked in the alveoli surrounding the bronchi and bronchioles. The walls of the bronchi and trachea show necrosis and infiltration with polymorphonuclear leukocytes, and their lumens are usually filled with exudate containing a predominance of these cells. Edema fluid in the alveoli and frothy pink material in the bronchi have been described in one case,¹⁶ which was complicated by chronic rheumatic heart disease and may have been the result of congestive failure. Necrosis and cellular infiltration of the walls of the pulmonary artery¹⁹ and of its smaller radicles¹⁶ have been noted. Acute splenic tumor and focal hepatic necroses have also been described.¹⁵ No inclusion bodies have been found in these cases.

It is interesting to note the similarity of the above description to those given for bronchopneumonia or "interstitial pneumonia,"^{20, 31, 32} "purulent bronchitis,"³³ influenza, psittacosis and other known virus diseases,²⁸ pneumonia due to the influenza bacillus⁵⁰ and pneumonia complicating measles, whooping cough and other diseases in man and animals.^{17, 49, 51}

Essentially the same pathologic processes were found by Adams and his co-workers^{20, 22} in the lung of infants dying of an acute epidemic respiratory disease mentioned earlier in the paper. In addition, these investigators noted acidophilic intracytoplasmic inclusion bodies in the bronchial epithelial cells. Similar inclusions were found in cells obtained by swabbing of the throats of infected infants, and of control infants and adults having contact with these cases. The presence of inclusion bodies is suggestive evidence of infection with a virus, but conclusive proof of virus etiology can be obtained only by the isolation of the virus and demonstration of its specific relation to the disease. Thus, intracytoplasmic or, more frequently, intranuclear inclusions have been found in the epithelial cells of infants and children following measles, influenza, whooping cough and a number of related infectious and noninfectious processes,^{17, 48, 49} but an etiologic relation has not been demonstrated satisfactorily.

ETIOLOGY

The etiology of atypical pneumonia has not been established satisfactorily. As pointed out above, this clinical syndrome may be produced by a number of known bacteria and viruses, and yet in the majority of the reported outbreaks in which studies were made, none of these agents were identified with the disease.

The usual laboratory procedures have yielded entirely negative results. Blood cultures are ordinarily sterile.¹⁶ Agglutinins are not demonstrable for the bacilli of typhoid fever, undulant fever, tularemia and supestifer infection, and blood smears reveal no malarial parasites.^{8, 16} Cultures of the sputum show the usual throat flora: *Streptococcus viridans*, *Neisseria catarrhalis*, staphylococci, *Str. haemolyticus*, diphtheroids and influenza bacilli.^{1-4, 7, 8, 10, 13-16, 21, 25, 52} Pneumococci have been found in more than half the cases by some investigators¹⁹ and infrequently by others,^{3, 14, 15} but in practically all the organisms are of the so-called "higher types," which are less pathogenic and more commonly found in carriers. Kneeland and Smetana¹⁵ considered the distribution of bacteria present in the respiratory tract of their cases to be essentially the same as that of normal persons. No tubercle bacilli or fungi are demonstrable.^{16, 25} The appearance of hemolytic staphylococci or streptococci in the sputum late in the disease as possible secondary invaders is probably not frequent, since it has been noted in only 3 cases.^{10, 52} Adams and his co-workers^{20, 22} reported no significant bacteriologic findings in their cases in infants.

A number of attempts have been made to isolate rickettsias or viruses from these cases. From Reimann's¹³ cases, Stokes, Kenney and Shaw⁵³ and Francis and Magill⁵⁴ obtained an agent that produced illness and pulmonary lesions in ferrets and mice for a few passages, but then apparently became less virulent and was lost. Neither the influenza nor the psittacosis virus was isolated, and the patients did not develop complement-fixing antibodies for the influenza virus.¹⁴ Enders, Sullivan, Hammon and Meakins⁵⁵ examined blood, sputum and nasopharyngeal washings from 11 of the cases reported by Murray,⁹ but in no case was a virus obtained. Brown⁵⁶ was unable to isolate rickettsias or a virus from various specimens, including pulmonary tissue from the fatal cases reported by Longcope.^{16, 21} As noted above, no inclusion bodies were seen in these cases. Negative results were also obtained in a variety of animals, and in chick embryos with autopsy material from the fatal cases in infants studied by Adams, Green, Evans and Beach,²² although inclusion bodies were seen. Blood and pharyngeal washings from 6 of Daniels's⁴ cases were inoculated by Dyer and Topping⁵⁷ into mice, guinea pigs and chick embryos with negative results.

Weir and Horsfall⁵⁸ have reported the isolation in the mongoose and in chick embryos of a filterable agent obtained from each of 4 patients with "acute pneumonitis." Production of pulmonary

lesions in mongooses was somewhat irregular, since some animals were apparently resistant to infection, and serial passage did not increase the virulence of the agent. By a rather laborious passage technic, it was found that the agent, when mixed with convalescent serums of the patients, produced a lower percentage of pulmonary lesions in the mongoose than when acute serums were similarly employed, indicating the development of neutralizing antibodies. A large variety of animals, including monkeys, were resistant to inoculation with the original material from the patients, as well as with pulmonary tissue from the infected mongoose. The agent was apparently not related to other known viruses producing respiratory disease.

Further work is necessary to clarify the etiologic situation in atypical pneumonia. Until this has been accomplished, diagnosis of the disease will remain uncertain. Differentiation should be made as completely as possible on the basis of laboratory tests to exclude the known viruses that can cause the same clinical picture, such as those of influenza A and B, psittacosis, meningopneumonitis,^{28, 59} ornithosis and rickettsias. Other conditions such as tuberculosis, typhoid fever, undulant fever, pneumococcal pneumonia, coccidioidomycosis, bronchiectasis, cancer, pulmonary infarction and atelectasis, must, of course, be considered in the differential diagnosis.

TREATMENT AND PREVENTION

The treatment of atypical pneumonia at present is entirely supportive or symptomatic, since no specific measures are known. The diet may be unrestricted or determined by the patient's appetite. The fluid intake, either orally or parenterally, should be maintained at 3000 to 4000 cc. per day or more during hot weather. Adams and his co-workers²² have stated, however, that infants with "primary virus pneumonitis" do not tolerate parenteral fluids well. Opiates, particularly codeine sulfate in $\frac{1}{2}$ -gr. or 1-gr. doses, are of value for cough, headache and generalized aching, but suppression of these symptoms may be difficult. Expectorants may be helpful when sputum is scant. Steam inhalations, with or without tincture of benzoin, or an increase in the humidity of the ward may give some relief. Abdominal binder and an ice cap may also be helpful. Reimann and Havens¹⁴ recommend that acetylsalicylic acid, acetophenetidin and aminopyrine be avoided because of the diaphoretic action of these drugs, particularly in cases in which sweating is an annoying symptom of the disease. Oxygen therapy, a tracheostomy or a nasal catheter being employed, usually relieves dyspnea and cyanosis. Postural drainage may be of value if the cough becomes productive.

of large amounts of sputum in the later stages of illness. Sprays or gargles of physiologic saline solution or weak sodium perborate solution may be employed, and a spray of 1 per cent aqueous solution of ephedrine may be used to relieve nasal obstruction. Enemas should be employed as indicated.

Transfusions have been recommended^{8, 22} Kneeland and Smetana¹⁵ have given a transfusion from a convalescent donor in 1 case, but the value of this specific therapy has not yet been established. The various sulfonamide drugs have been used in a considerable number of cases,^{3, 4, 14, 10, 22} without any significant effect on the course of the disease. Indeed, in some cases, the reactions to these drugs have materially increased the discomfort of the patients.¹⁴ Pneumococcal antiserums have been tried in a few cases, without evident success.¹⁴ In most cases, a prolonged period of convalescence is required. Complications should be treated as indicated.

Only general preventive measures are available in attempts to stop the spread of atypical pneumonia. The infection is apparently not highly communicable, but the large number of cases occurring in medical personnel caring for these patients indicates contact spread, possibly by droplet infection. Strict isolation of the patients is recommended.^{14, 21} Masks and gargles may be of value.²⁰ Prevention by immunization must await the isolation of the etiologic agent.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28361

PRESENTATION OF CASE

A forty-year-old man was admitted to the hospital because of bouts of abdominal pain.

Five months before admission, the patient experienced a sudden attack of pain without anorexia or nausea, sharply localized to the right lower quadrant. This episode lasted three days. No change in bowel habits had occurred, and on examination, there was only mild tenderness in the right lower quadrant. A month later, similar symptoms recurred, and an "infected appendix" was removed at a community hospital. At operation, an inflammatory mass of undescribed size was attached to the ileum several inches from the ileocecal valve. Following this, the patient made an uneventful recovery. Five weeks later, symptoms recurred, but at this time, the patient complained of generalized gas pains and soreness in the epigastrium. These were relieved by an enema, but recurred once during the succeeding month with an associated left-lower-quadrant pain. This time, relief was obtained from a topical application of heat. No changes in stool habits or characteristics were noted.

The family and past histories were irrelevant.

Physical examination revealed a rather thin man in no obvious distress. The heart and lungs were normal. A firm, movable "egg sized" tender mass was felt in the right lower quadrant several inches to the side of the umbilicus. Rectal examination was negative.

The blood pressure was 125 systolic, 80 diastolic. The temperature was 98.6°F., the pulse 90, and the respirations 20.

Examination of the blood revealed a hemoglobin of 14 gm., and a white-cell count of 9800 with 88 per cent polymorphonuclears, 8 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils. The blood Hinton reaction was negative. Urine and stool examinations were negative.

A barium enema passed to the cecum without delay and entered the terminal ileum. Approximately 6 cm. from the ileocecal valve, there was a localized area of ulceration on the lateral wall of the terminal ileum, with rather sharp margins. In addition to the area of ulceration, a soft-tissue mass appeared to be pressing into the

lumen of the bowel. There was a moderate amount of mucosal swelling. The ileum proximal to the lesion was not dilated. A single diverticulum was seen in the midtransverse colon.

Operation was performed on the ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD HAMLIN, JR.: I think we had better start with the x-ray films.

DR. AUBREY O. HAMPTON: The radiologist can not often give a report so definite as this, but these films show why he was so certain that the ileum was ulcerated—there is a notchlike projection here simulating a gastric ulcer. It is a deep ulcer, 1 cm. in diameter, and there is an area of rigidity around it that might also be shallowly ulcerated, 3.5 to 4 cm. in width. The reason the radiologist said that there was a mass pressing into the ileum is that there do seem to be a large number of mucosal folds in the area of this lesion which are not exactly normal.

DR. HAMLIN: Could the effect be produced by rigidity of the bowel?

DR. HAMPTON: I think the bowel must have been rigid near the ulcer over an area about 3 cm. in length.

DR. HAMLIN: The patient complained of intermittent pain, some of which might be classed as a local peritoneal irritation, some of which was quite likely due to low-grade intestinal obstruction, and some of which I cannot account for. I should rather like to know—he is described as a thin man but we are not told whether he had lost weight or increased fatigability—whether or not this was a chronic lesion that had produced effect. The examination tells us nothing more than that there was a mass in the right lower quadrant. The laboratory data reveal nothing of any significance except that there was no evidence of real acute inflammation, although perhaps one could call this a low-grade inflammatory process. The written x-ray report puzzled me more than anything else. One other thing that bothered me was the description of the inflammatory mass noted at previous operation at the time of appendectomy because of the use of the word "attached." It sounds rather like a tumor that was protruding from the wall of the intestine.

Several conditions might have been responsible for this lesion. The first thing I thought of was the question of foreign body. A foreign body which impinged on the mucosa of the bowel and became imbedded, could produce such a low-grade inflammatory process, although Dr. Hampton's comments make it seem rather less likely. The chief objection is the elapsed period of five

months since the onset of symptoms, which is rather a long time to associate with a foreign body in such intimate contact with the bowel.

The patient had a tumor. Could the tumor have been neoplastic? The carcinomas and carcinoids of the small bowel are rare. The one or two that I have seen certainly produced no picture such as this. They are mostly annular and constricting and much more likely to cause obstruction than ulceration of this nature. The one tumor that seems most likely to produce a picture of this sort rather than any other is lymphoma, and that I cannot exclude. One would think that lymphoma would be more likely to cause a secondary anemia and blood in the stools, which this man did not have.

A Meckel's diverticulum containing gastric mucosa occurred to me as a possibility. The lesion is certainly rather closer to the cecum than one would expect, and a study that Wallace¹ made in this hospital revealed that when the symptoms from a Meckel's diverticulum could be attributed to the presence of gastric mucosa they resulted before the age of twenty, and this man was well beyond that. Accordingly, we can probably exclude any effect of a Meckel's diverticulum.

When one considers the diseases of the ileum, one immediately thinks of ileitis. Could this have been an atypical form of regional ileitis? Crohn and Berg² state that blood almost invariably is noticed in the bowel movements. However, of the 33 cases of regional ileitis in the series reported by Warren and Miller³ in this hospital, only 2 showed blood in the stools. Diarrhea is one of the most important symptoms of regional ileitis; yet in this same series, 6 patients had no evidence of diarrhea when the diagnosis of ileitis was made. Obstruction is not an obstacle, because in studies of ileitis there may be no x-ray evidence of obstruction such as one would expect from constriction of the inflammatory lesion. The one factor that is perhaps more of an obstacle than any of the others is that fistulas did not result following the appendectomy. All the fistulas that have been seen in this hospital in cases of regional ileitis have resulted from operation.

There are several other lesions or diseases that might possibly produce this picture, most of which are rare and are not worth the time to discuss. I cannot exclude a lymphoma or an atypical regional ileitis, and of the two I should favor the latter.

DR. HAMPTON: I was just about to say that I do not believe we have seen anything similar to this in regional ileitis. A local single ulceration would be most unique, I should think; and then

it does have the picture of a tumor by x-ray—the shell-like margin around the area of stiffening. This penetrating ulcer simulating a gastric ulcer is the part that we did not like because we had not seen such a picture. It seemed as if there might be a “nigger in the woodpile,” but I think the diagnosis on x-ray study was lymphoma.

A PHYSICIAN: What would you say about carcinoma?

DR. HAMPTON: It does not produce ulceration.

DR. TRACY B. MALLORY: I should emphatically say that we have never seen ulceration with carcinoid in the ileum. On the other hand, carcinoid frequently involves regional lymph nodes and would account for pressure from an extrinsic lesion in addition to signs of intrinsic mass.

DR. LELAND S. MCKITTRICK: We thought there was a possibility that there was no ulcer—in other words, that this was infolding of the mucosa.

DR. HAMPTON: No one suspected that. We thought it must be ulcerated.

DR. MCKITTRICK: Just to be sure of the written impression of the X-ray Department, it says: “This can be either inflammatory process or tumor. If tumor is the cause, the most likely possibility would be carcinoma or carcinoid.” That may not represent the impression of the X-ray Department, but that is the written interpretation.

DR. HAMPTON: That is the impression of an individual. The majority of the department staff did not agree with him.

DR. MCKITTRICK: When this man was sent to me, I thought he had regional enteritis from the story. I cannot find my preoperative diagnosis, and I am not absolutely sure of the diagnosis we operated under, but I think it was carcinoma even though the location was unusual. There is no reason why it could not occur there, and the x-ray picture was entirely consistent, as was the clinical story. The patient did have a lesion that was perfectly characteristic of a carcinoma—a firm hard indurated mass, classic in every way. The unusual part about it was the large mass of non-broken-down lymph nodes extending along the root of the mesentery. Further exploration showed that the liver and spleen were normal; there was nothing else within the abdominal cavity that I could find. We did a right colectomy.

A PHYSICIAN: Including the terminal ileum, of course?

DR. MCKITTRICK: Yes; the terminal ileum and the right colon around to the midtransverse colon were removed. That was the only way we could include the lymph nodes at the root of the mesentery without interfering with the blood supply.

CLINICAL DIAGNOSIS

Carcinoma of terminal ileum?
Terminal ileitis?

DR. HAMLIN'S DIAGNOSIS

Regional ileitis?
Lymphoma?

ANATOMICAL DIAGNOSIS

Malignant lymphoma, lymphoblastic type, of ileum.

PATHOLOGICAL DISCUSSION

DR. MALLORY: We were puzzled by this specimen when it came to the laboratory. When it was opened, there was an ulcerative tumor of the bowel looking like carcinoma, and a mass of lymph nodes in the mesentery, some of them matted together. Cutting across this mass of nodes, we found them to consist of soft pinkish tissue that showed no signs of necrosis or breaking down, so that the nodes were very unlike carcinoma and very suggestive of lymphoma. On the other hand, our experience with lymphoma in the bowel is that the regional lymph nodes are very seldom involved even when grossly enlarged. They ordinarily show simple hyperplasia and no lymphomatous infiltration, whereas it was obvious that these nodes were neoplastic. Microscopic examination showed that it was lymphoma of an undifferentiated lymphoblastic type, and the same picture was present both in the bowel wall and in the regional lymph nodes.

Since operation, this patient has been given intensive x-ray treatment. I do not know whether the tumor has recurred.

DR. MCKITTRICK: I heard from the patient's physician recently. The patient was reported to be doing well six months after the operation.

DR. MALLORY: A significant proportion of these lymphomas of the bowel, of course, do remarkably well after resection. We have cases that have run seven, nine and eleven years after resection, and they are therefore well worth operating on.

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CASE 28362

PRESENTATION OF CASE

A forty-four-year-old lumber salesman was admitted to the hospital because of periumbilical pain, nausea and vomiting.

Ten weeks prior to admission, on the morning following an evening of heavy eating, he suffered the first attack of biliousness and diffuse intermittent abdominal ache, nausea and vomiting. His physician treated him with belladonna and paregoric, and the symptoms disappeared after five days. The patient was well until ten days before admission, when similar symptoms occurred, and several days later he noted for the first time continuous aching pain in the left side of the abdomen. This was partially relieved when he vomited some "dark fluid."

X-ray studies at another hospital were said to have shown partial obstruction in the midportion of the small intestine, esophageal varices, a small liver shadow and diverticula in the lower portion of the descending colon. After these studies were made, the patient improved and remained well until twenty-four hours prior to admission to this hospital. At this time, two or three hours after eating, the usual symptoms of biliousness, nausea and abdominal ache recurred and were relieved by vomiting. The patient was symptomless on the day of admission. The vomitus had never contained blood, and there had been no changes in the stool characteristics.

The family history was irrelevant.

At seventeen years of age, the patient had peritonitis secondary to a perforated appendix, and this required drainage for seven weeks. Following this, he developed phlebitis in both legs, which had intermittently been swollen ever since. Thirteen years before entry, a sore left leg and hip developed. Soon after this, the patient had an attack of severe chest pain and dyspnea, interpreted as pulmonary infarction. The cardiorespiratory history was otherwise irrelevant.

The patient was said to have consumed four or more highballs each day. His diet included meat, milk and vegetables; however, he usually ate only one meal a day.

Physical examination revealed a well-developed and well-nourished man in no discomfort. Examination of the heart and lungs was negative. The veins over the upper and lower abdomen were prominent. No abdominal masses were felt, and there was no tenderness. Rectal examination was negative. There was slight edema of the left leg, and pigmentation of both lower legs.

The blood pressure was 118 systolic, 68 diastolic. The temperature was 99°F., the pulse 89, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,000,000 with a hemoglobin of 78 per cent, and a white-cell count of 9500. Examination of the urine was negative.

On the second hospital day, soon after a meal of toast and coffee, the patient noticed the onset of slightly crampy midabdominal pain, which increased in severity during the day. The patient retched but was unable to vomit. Physical examination at this time was negative.

That evening, he vomited several hundred cubic centimeters of slightly green, watery material and obtained immediate relief. There was moderate diffuse tenderness, maximum to the right of the umbilicus, and spasm of the entire abdomen.

The patient vomited several times during the next day. The white-cell count was found to be 40,700 and, five hours later, 48,000. At this time, there was definite tenderness in the right upper quadrant, and operation was immediately performed.

DIFFERENTIAL DIAGNOSIS

DR. REGINALD H. SMITHWICK: So far as I can see, there was no opportunity to take any x-ray films on this patient before he was operated on, at least in this hospital.

The picture given by the history is that of a well-nourished, middle-aged man who, aside from slight secondary anemia, appeared to be in good condition on entry to the hospital. The past history is important in that he had an operation for appendicitis, with drainage, twenty-seven years previously. There is evidence that this was followed by a deep thrombophlebitis, with exacerbation four years later. This might be the explanation for dilated veins over the lower chest and abdomen rather than cirrhosis of the liver resulting from indiscretions of eating and drinking. In any event, the relation of either an old deep thrombophlebitis or cirrhosis to the present illness is not clear.

The present illness consisted of four attacks of crampy, periumbilical pain, associated with nausea and vomiting over a ten-week period, the first lasting five days and the second a shorter period—being followed, however, by less severe, but rather persistent abdominal discomfort. The third attack was sudden and severe but of short duration, and the fourth was sudden in onset, with increasing severity, persistent nausea, tenderness, spasm and a striking rise in the white-cell count. No mention is made of distention or abnormal peristalsis. The nature, location and severity of the pain, coupled with the information from the x-ray examination elsewhere, revealing partial obstruction, suggest that the lesion was located in the small intestine.

Other conditions that might possibly cause these symptoms are pancreatitis, disease of the biliary tract, with subsequent rupture of the gall bladder, possibly a perforated peptic ulcer, diverticulitis with perforation and appendicitis. Presumably, the appendix was removed twenty-six years

previously, although one cannot be certain that that was so. Diverticulitis with perforation is rare, except in the sigmoid. No mention is made of fever, which should be considerable if the cause of the symptoms at the time of the operation was primarily an inflammatory process, although it is possible that peritonitis was present at the time of operation.

The most probable diagnosis is obstruction of the midportion of the small bowel, associated with interference of the blood supply. Mesenteric thrombosis might cause such a picture, but the pain is likelier to continue and does not explain four attacks in ten weeks, with spontaneous recovery from the first three. In view of the previous operation, partial obstruction from an adhesive band culminating in obstruction should be placed first as the cause of this man's difficulties. The symptoms, however, could be equally well explained by recurring intussusception related to tumor, polyp or stricture of the small bowel, resulting in necrosis of the invaginated bowel.

DR. LELAND S. MCKITTRICK: Do you exclude an acute pancreatitis? You passed over that very quickly, Dr. Smithwick. Do you believe it is usually so easy to rule it out in such a case?

DR. SMITHWICK: It seems to me that, with an acute pancreatitis, it is unusual to have so many attacks as this man had, although we do know that it can be recurrent. Acute pancreatitis simulating small-bowel obstruction, I believe, was the first disease mentioned in the differential diagnosis; it should be included. I should expect that more would have been said regarding the general serious condition of the patient, with more evidence of shock and collapse, and I should not expect the white-cell count to be so elevated as this man's was. It would be much lower in acute pancreatitis, and there would be a good deal more evidence of collapse than I gather from the clinical description in this case. I think acute pancreatitis is a very definite possibility, but I do not put it first.

DR. TRACY B. MALLORY: Does anyone want to hazard an opinion on the relation of the four highballs a day to the esophageal varices? That is a rather crucial figure.

DR. MCKITTRICK: I suppose that would depend on the highballs. Many people would believe that four a day would do it.

DR. AUBREY O. HAMPTON: They said that he had a small liver, did they not?

DR. SMITHWICK: I was rather inclined not to lay much stress on that because it seemed to be information that was obtained elsewhere and was not confirmed by evidence accumulated during the present illness.

DR. MCKITTRICK: I rather had the impression that obstruction had a much more abrupt and

more positive onset than this. I should be a little hesitant to expect strangulative obstruction, because of the past history. Also, the story of the last month alone would not fit into my concept of strangulated small-bowel obstruction, but I am probably being educated.

DR. SMITHWICK: So far as I can estimate from the history, in the course of twenty-four to thirty-six hours, this man passed from a healthy person to one who was desperately sick, with no mention of fever or other evidence of an inflammatory process. That seems quite abrupt and severe to me.

DR. MALLORY: The temperature on the first day was 99.5°F., and on the second 98°F.

DR. SMITHWICK: With increasingly severe pain of rather sudden onset, I gather from the description of the periumbilical crampy midline abdominal pain.

DR. MCKITTRICK: But not bad.

DR. SMITHWICK: Not bad at the moment it started, but increasingly severe, followed by generalized tenderness and spasm.

DR. REED HARWOOD: Did you ask if the esophageal varices and small liver could be linked with the present symptoms?

DR. MALLORY: No; but I should be interested if anyone had a theory by which they could be explained. What should you say, Dr. Hampton, about the reliability of the radiologist's observation of varices?

DR. HAMPTON: If the examination is carried out in a Grade A hospital by a Grade A man, the observations should be very accurate. I wager that this patient had cirrhosis of the liver, because I know who made the examination.

A PHYSICIAN: Dr. Fuller Albright had a patient with four attacks of pain simulating gall-bladder disease and various other things who finally had a severe venous thrombosis of the small bowel.

DR. SMITHWICK: I was not aware that cirrhosis of the liver ever resulted in mesenteric venous thrombosis. If so, that would be a likely sequence of events in this case.

PREOPERATIVE DIAGNOSIS

Gangrene of bowel.

DR. SMITHWICK'S DIAGNOSIS

Obstruction of midportion of small bowel, with occlusion of its blood supply.

ANATOMICAL DIAGNOSES

Mesenteric and portal thrombosis, recent.

Venous infarction of small intestine, acute.

Thrombosis of splenic vein, old.

Thrombosis of femoral and popliteal veins, old, bilateral.

Esophageal varices.

Splenomegaly, slight.

Peritonitis, acute.

Operative wound: appendectomy.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was explored. When the abdomen was opened, the operator felt a mass that was surrounded by omentum. On peeling back the omentum, he found that the mass consisted of loops of discolored small intestine, about 150 cm. in length and matted together by fibrinous adhesions. All the veins in the mesentery leading from these loops were thrombosed. The surgeon, who also examined and felt the liver, reported that it was small and that it was finely granular and tough. He noted a very hard cord, which extended from somewhere near the hilum of the liver across the abdomen in the direction of the spleen, and suggested an old thrombosis of the splenic vein.

At autopsy, two days later, the latter observation proved to be entirely correct. There was complete obliteration of the splenic vein, obviously going back many years; it was completely organized and partially recanalized. The spleen was fibrotic, but not much enlarged. There were esophageal varices, but the liver seemed entirely smooth and softer than normal; microscopically, there was no cirrhosis. The acute thrombotic process in the mesenteric veins had, in the intervening two days, spread to involve the entire portal system. Every peripheral branch of the portal vein was thrombosed, as was the main portal vein, and the thrombi extended well up into the portal radicals of the liver. There were old and dense fibrous adhesions about the cecum in the region of the appendix, but none of the adhesions could have obstructed any loop of small bowel, so that we have nothing at autopsy to account for the intermittent attacks except the thrombotic process; accordingly, I think we must assume that the thrombosis had occurred in stages and did account for the recurring episode.

DR. MCKITTRICK: Warren and Eberhard* some years back, from a study of venous mesenteric thrombosis, concluded that one could have recurring episodes without necrosis of the bowel, many times culminating in episodes of this kind. The recurring multiple episodes in the past are entirely consistent with it.

DR. MALLORY: I had forgotten that. I suppose that it could occur with venous thrombosis but probably never with the arterial type of mesenteric thrombosis.

*Warren, S., and Eberhard, T. P. Mesenteric venous thrombosis. *Surg., Gynec. & Obst.* 61:102-121, 1935.

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INDUSTRIAL MEDICINE IN MASSACHUSETTS

THE announcement of the Committee on Industrial Health that appears elsewhere in this issue of the *Journal* focuses attention on the medical aspects of a dislocation in civil life that is of growing importance. The industrial expansion of the Nation is now of such proportions that it is said to be creating urgent problems in many areas. As yet, no one has actually conducted a survey with sufficient care to give an accurate picture, but it is well known that whole cities and towns for the sole purpose of wartime production are rapidly springing into existence. How quickly and how completely they may be provided

with the civilized accoutrements of the older cities and towns in these days of shortages and priorities is an open question. Already, established cities and towns are learning that they must sacrifice many of the things they formerly considered essential, and these sometimes include medical services. For example, the Procurement and Assignment Service has not hesitated to classify the only physician in a small town as available when such a town is relatively close to others from which doctors can be obtained when needed. This and other comparable privations are beginning to create an appreciation of the immensity of the task. To what extent industrial demands, over and above the tremendous military needs, for medical service will still further deplete civilian resources remains to be seen, but it is both prudent and timely that steps are being taken to prepare for whatever dislocation becomes necessary.

In Massachusetts, the natural geography is such that large areas cannot be altogether remote from medical and hospital services. There are a larger number of both physicians and hospital beds per unit of population than in most other sections of the country, and expansion generally consists in the enlargement of previously existing plants or facilities. Furthermore, the State Department of Labor and Industries is well organized and alert, and its Division of Occupational Hygiene is nationally recognized as a leader in industrial medicine. And, finally, certain members of the State Department of Public Health are especially interested in the potentialities of industrial health. In other words, Massachusetts appears to be in a position to solve whatever problems arise, and to do this with already existing machinery. If so, she will be more fortunate than other states, where the resources are more meager and the load relatively greater.

During the early days of the late depression, President Ernest M. Hopkins, of Dartmouth College, insisted that times of stress and change were times of opportunity for those who could foretell and foresee the trends of the future. Not only did this prove to be so, but many who set their courses, not by foreseeing the future, but by mere

expediency, lived to reap the benefits of currently changing fortunes. In ordinary times, an expanding and medically minded industry would reach for a young physician—a man who could grow and mature with the business. Today, however, the opportunity is open to all. It is likely that those who have done best in private practice will do best in industrial practice, and this is fortunate because in Massachusetts the greatest opportunity lies in serving small plants, in which three quarters of the workers of the State are employed. The medical service for these small plants is almost certain to develop as a part-time activity of the practicing physician, rather than as a full-time assignment. This circumstance also places industrial medicine where it belongs—not in the group of specialties, but in the group of activities that constitute the general practice of medicine and surgery.

VIRUS PNEUMONIA AND ORNITHOSIS

THE atypical pneumonias of varying severity that fail to yield significant bacteriologic agents and also fail to show the characteristic favorable response to sulfonamide drugs continue to be a challenge to physicians and laboratory investigators. At present, the group may be said to constitute a fairly well-defined clinical syndrome. The meager positive results of laboratory studies, however, have already pointed to the diversified character of the etiologic agents in cases that present very similar clinical findings. The situation is probably analogous to that found in primary lobar pneumonia, which is now known to consist of a group of specific infectious diseases caused by many organisms, of which certain types of pneumococci are the most frequent.

The possible significance of the rickettsia of Q fever and of the virus that Weir and Horsfall encountered when they used the mongoose for the study of materials from human cases has already been discussed in the *Journal*.^{*} Intensive work on

this problem is continuing in a number of laboratories throughout the country, and also by groups of investigators in the Army and Navy. The present status of the problem is summarized in this and the preceding issue of the *Journal*.

Two important points brought out in these reports are worth emphasizing. The first concerns terminology. The diagnosis "virus pneumonia" is now widely used both in verbal discussions and in many written reports, in spite of the failures to demonstrate filterable viruses in almost all the cases so labeled. Many writers, to avoid this possibly misleading designation, have resorted to the use of a number of terms, each of which emphasizes some clinical, roentgenologic or, sometimes, pathologic feature of the disease. For purposes of classification, however, there are serious objections to such terminology. The designation recently recommended to the Surgeon General for use in the United States Army is, "*primary atypical pneumonia, etiology unknown*," and this seems to be the most suitable one suggested thus far. It implies that an earnest effort has been made to rule out the known etiologic agents, particularly bacteria. It also implies that the known nonbacterial causes of similar respiratory infections, such as influenza, psittacosis and Q fever, have been considered and that they were either ruled out or thought to be unlikely causes on clinical or epidemiologic grounds.

The second point of interest is the increasing number of reports of the finding of a psittacosis-like virus in some cases of this group, as well as the association of these cases with pigeons and domestic fowl. The studies of a number of workers, including Meyer, Pinkerton, Francis, Eaton and their collaborators, have indicated that the virus concerned is very widespread among the pigeons in this country wherever it has been sought. It has been isolated from a significant number of birds in many pigeon lofts, and serologic studies have indicated very widespread latent and subclinical infection. Furthermore, evidence of infection has been found in the pigeons

^{*}Editorial. Virus pneumonia and Q fever. *New Eng. J. Med.* 224:36, 1941.

in Central Park and in other parts of New York City.

Cases of atypical pneumonia, clinically similar in all respects to those described by many writers, have occurred in pigeon breeders and also in persons having contact with ordinary street pigeons. Serologic evidence of infection has also been found in many pigeon breeders who have had no clinical symptoms. Infections, both latent and manifest, have been observed in barnyard fowl, including chickens, ducks and turkeys, but not in wild birds, and cases ascribable to contact with sick fowl have also occurred.

Meyer has suggested that such infections be called "ornithosis" and that the atypical pulmonary infections associated with them be termed "ornithotic pneumonia." Thus, another group of cases of atypical pneumonia has been removed from the category of "etiology unknown." The diagnosis may be established by the demonstration of the virus by means of mouse inoculation of sputum or lung material obtained at the height of the disease; or infection with the virus may be demonstrated by an increase in the titer of antibodies by complement-fixation tests for the virus during convalescence. There are some difficulties involved in both methods because of the close immunologic relation between the psittacosislike virus of pigeons and certain naturally occurring viruses of mice, as well as the virus of lymphogranuloma venereum. Since subclinical infection with the last virus has been demonstrated recently, this difficulty is more than merely theoretical.

It should be borne in mind, however, that the number of human cases of atypical pneumonia in which the pigeon virus has been demonstrated either by direct isolation or by immunologic tests is still very small in comparison with the number of cases in which it has been sought. In many, if not most, proved cases, a history of contact with pigeons, and often with sick ones, could be elicited. In the great majority of cases of characteristic atypical pneumonia, the etiology still remains unknown. It is hoped that the intensive studies now

in progress will remove a greater proportion of these cases from this category and place them in the group of cases with known etiology.

MEDICAL EPONYM

VON RECKLINGHAUSEN'S DISEASE

This disease forms the subject matter of a monograph by Friedrich Daniel von Recklinghausen (1833-1910), professor at Strassburg, entitled *Über die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuomen* [Multiple Fibromas of the Skin and Their Relation to Multiple Neuromas] (Berlin, 1882), which appeared as a part of the *Festschrift* commemorating the twenty-fifth anniversary of the foundation of the Pathological Institute in Berlin and dedicated to Rudolf Virchow. A portion of the translation follows:

From the results of these studies, I may assert that these little tumors are fibromas, which are formed in the small nerves of the skin after the same fashion as the fibromas in the larger trunks. . . . In respect to their origin, the multiple, soft fibromas of the skin have arisen from neuromas, hence *neuromatous fibromas* or *neurofibromas*.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON INDUSTRIAL HEALTH

Following the announcement that called attention to the distribution of the *Manual on Industrial Health for Defense* in the July 30 issue of the *Journal*, the Committee on Industrial Health received several inquiries from physicians seeking openings in industrial medicine. Because the committee had no ready method of meeting these inquiries, on August 17, it voted to "constitute itself as an agency to gather what information it can concerning doctors who may be available for industrial work and also information concerning possible placements for such doctors, working, of course, in close co-operation with the Procurement and Assignment Service and with due regard for other than industrial need for medical service."

If this function is to be developed, it will be necessary for the committee to possess certain information concerning physicians who are ready to undertake industrial practice. The committee is therefore preparing a registration form that will be forwarded to any Massachusetts physician who wishes to record himself or herself as a candidate

for industrial assignment, as well as to state the conditions under which he or she would be willing to accept such an assignment. The committee may be addressed for this purpose at 8 Fenway.

DWIGHT O'HARA, *Chairman*

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY: GONOCOCCAL SEPTICEMIA, PELVIC PERITONITIS AND THROMBOPHLEBITIS, FOLLOWED BY LAPAROTOMY AND DEATH

In a twenty-nine-year-old primipara who had been treated intelligently and adequately during her pregnancy, labor was induced by rupture of the membranes two weeks from term because of mild toxemia, a blood pressure of 160 systolic, 110 diastolic, and slight albuminuria. The past history was irrelevant. Labor started immediately after the membranes had been ruptured and progressed normally to full dilatation. The patient was delivered by low forceps because of the prolonged second stage and because of maternal fatigue. The third stage was complicated not by hemorrhage but by the fact that the placenta did not separate. During the first twenty-four hours after delivery, several 1-cc. doses of pituitary extract were given to stimulate separation of the placenta. Because this did not accomplish separation, the uterus was invaded manually under very strict asepsis, the line of cleavage between the placenta and the uterine wall readily found, and the placenta and membranes manually delivered intact. There was no hemorrhage during or following this procedure. A chill followed within the first twenty-four hours after delivery of the placenta, a septic temperature developed, and in spite of repeated transfusions and chemotherapy the patient died two weeks later. Gram-negative intracellular diplococci were found in a smear from the cervix, and repeated gonococcal-fixation tests were reported positive. Two days before death, a laparotomy was undertaken for the purpose of draining a pelvic abscess. Autopsy showed general septicemia, pelvic cellulitis, acute pelvic peritonitis, thrombophlebitis of the right common iliac vein and an infarct in the right lung.

Comment. The operative conduct of this case cannot be criticized. Induction of labor by rupture of the membranes during the last month of pregnancy, in the presence of increased blood pressure and albuminuria, is certainly advisable treatment. The fact that labor immediately followed rupture of the membranes shows that the cervix was favorable for induction. The delayed second stage had no necessary connection with this induction. The question of leaving a placenta in

situ for twenty-four hours or longer after the birth of the baby is a problem that is treated differently in various clinics. In the absence of hemorrhage, it should certainly be safe to leave the placenta as long as it was left in this case before manual removal is attempted. It is logical to conclude that in patients of this sort who do not bleed after delivery the placenta has remained entirely attached. It is in cases in which partial attachment and partial separation occur, accompanied by free hemorrhage, that the placenta must be immediately attended to. In this case, the uterus was invaded under strictest asepsis for the purpose of making a diagnosis. This might have been a completely adherent placenta and one that was an accreta, which could not have been removed manually. The diagnosis of this condition can be made only by intrauterine manipulation. Had placenta accreta been diagnosed, the treatment would have been transfusion and hysterectomy. In this case, since there was apparently no bleeding during or following the operation and since the line of cleavage was easily recognized, the placenta was a mildly adherent one. Because gonococci were isolated in a smear from the cervix and gonococcal-fixation tests were positive during convalescence, the bacteriologic cause of the infection is demonstrated beyond argument. The trauma of removing this placenta may well have been a contributing factor. There is nothing to commend the laparotomy that preceded this death by two days. Had a pelvic abscess been apparent, it should have been drained posteriorly.

DEATH

JACOBY — RUDOLPH JACOBY, M.D., of Newtonville, died August 20. He was in his fifty-third year.

Born in Newburyport, Dr. Jacoby received his degree from Boston University School of Medicine in 1911. He was professor of dermatology and syphilology at Boston University School of Medicine, and was a member of the American Academy of Dermatology and Syphilology and the New England Dermatological Society, and a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and two sons survive him.

MISCELLANY

NOTE

The Medical Library Association held its forty-fourth annual meeting in New Orleans on May 7-9, 1942. The officers elected for the coming year are as follows: Mary Louise Marshall (Tulane University), president; Dr. John F. Fulton (Yale University), vice-president; Frida Pliefke (Mayo Clinic), secretary; and Bertha B. Hallam (University of Oregon), treasurer.

(Notices on page viii)

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RHEUMATOID ARTHRITIS ASSOCIATED WITH SPLENOMEGALY AND LEUKOPENIA*

ROBERT H. TALKOV, M.D.,† WALTER BAUER, M.D.,‡ AND CHARLES L. SHURT, M.D.

BOSTON

IN 1924, Felty¹ reported 5 cases of chronic arthritis in adults, with associated splenomegaly and leukopenia. The patients ranged from forty-five to sixty-five years of age and included 3 men and 2 women. All had experienced marked weight loss. Two had low-grade pyrexia. All showed a yellowish-brown pigmentation of the skin, usually confined to the exposed surfaces. Three patients exhibited enlarged lymph nodes, but none hepatomegaly. The arthritis was neither widespread nor severe. Roentgenograms in 3 cases revealed "infectious arthritis"; in another, no articular changes were noted. Leukopenia, with white-cell counts varying from 1000 to 4200, was a striking feature in each case. Four of the 5 patients had a mild secondary anemia. Felty suggested either that the triad represented a pathologic process caused by a noxa that concurrently affected the spleen, blood and joints or that the splenomegaly and leukopenia were entirely unrelated to the arthritis. Unfortunately, no pathological studies were obtained. Since this communication, a number of reports relating to patients with arthritis, splenomegaly and leukopenia have appeared; most of them have been referred to as cases of Felty's syndrome.

Having encountered this triad from time to time during the last thirteen years, we wish to place on record some of our observations. We shall first present the clinical data and autopsy findings of a case very similar to those described by Felty. We shall next attempt a critical analysis of this syndrome based on our clinical experi-

ence and a review of the pertinent literature, as well as to point out the various pitfalls that may be encountered if the term "Felty's syndrome" is used indiscriminately. Finally, we shall give our reasons for rejecting this term in favor of the more accurate designation, "rheumatoid arthritis."

CASE 1. Mrs. J. K. (MGH 13242), a 52-year-old woman, entered the hospital because of increasing weakness during the previous 3 months. For the past 6 months she had had arthritis involving primarily the knees, feet and spine. Constitutional symptoms were moderate except for marked weight loss. She had lost 15 lb. (7 kg.) in the last 1 year before entry, and anorexia had been present for 6 months. Five years before entry, a goiter was discovered, and dietary iodine was prescribed.

At the time of admission, there was no evidence of infection. Findings were pallor, signs of anemia, enlargement of the spleen and of the lymph nodes, enlargement of the thyroid gland, enlargement of the heart, enlargement of the liver, enlargement of the lungs, enlargement of the kidneys, enlargement of the adrenals, enlargement of the ovaries, enlargement of the uterus, enlargement of the prostate, enlargement of the testes, enlargement of the seminal vesicles, enlargement of the bladder, enlargement of the rectum, enlargement of the sigmoid colon, enlargement of the cecum, enlargement of the appendix, enlargement of the gallbladder, enlargement of the pancreas, enlargement of the salivary glands, enlargement of the parathyroid glands, enlargement of the thymus, enlargement of the spleen, enlargement of the liver, enlargement of the lungs, enlargement of the kidneys, enlargement of the adrenals, enlargement of the ovaries, enlargement of the uterus, enlargement of the prostate, enlargement of the testes, enlargement of the seminal vesicles, enlargement of the bladder, enlargement of the rectum, enlargement of the sigmoid colon, enlargement of the cecum, enlargement of the appendix, enlargement of the gallbladder, enlargement of the pancreas, enlargement of the salivary glands, enlargement of the parathyroid glands, enlargement of the thymus.

Examination of the blood showed a hemoglobin of 10.0 g. per 100 cc., a red-cell count of 4,500,000 per cu. mm., a white-cell count of 4,000 per cu. mm., and a platelet count of 150,000 per cu. mm. The sedimentation rate was 10 mm. per hour. The urinalysis was negative. The x-ray examination of the joints showed evidence of chronic arthritis.

Examination of the spleen showed a normal-sized spleen. The liver was normal in size. The lungs were normal. The kidneys were normal. The adrenals were normal. The ovaries were normal. The uterus was normal. The prostate was normal. The testes were normal. The seminal vesicles were normal. The bladder was normal. The rectum was normal. The sigmoid colon was normal. The cecum was normal. The appendix was normal. The gallbladder was normal. The pancreas was normal. The salivary glands were normal. The parathyroid glands were normal. The thymus was normal. The spleen was normal. The liver was normal. The lungs were normal. The kidneys were normal. The adrenals were normal. The ovaries were normal. The uterus was normal. The prostate was normal. The testes were normal. The seminal vesicles were normal. The bladder was normal. The rectum was normal. The sigmoid colon was normal. The cecum was normal. The appendix was normal. The gallbladder was normal. The pancreas was normal. The salivary glands were normal. The parathyroid glands were normal. The thymus was normal.

*From the Medical Clinic of the Massachusetts General Hospital, the Department of Medicine Harvard Medical School, and the Massachusetts Department of Public Health Boston.

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†Assistant in medicine, Harvard Medical School, graduate assistant in medicine, Massachusetts General Hospital.

‡Associate professor and tutor in medicine, Harvard Medical School, physician, Massachusetts General Hospital.

§Instructor in medicine, Harvard Medical School, assistant physician, Massachusetts General Hospital.

stools did not contain occult blood. The diagnosis of a primary blood disease could not be established. Roentgenologic examination showed marked narrowing of the knee joints, second and third metacarpophalangeal articulations and both wrists. Bony atrophy was prominent. The knees also showed subluxation and extensive marginal proliferation, with spur formation at the tendon attachments. The gastrointestinal and genitourinary tracts were normal radiologically. Attempts to demonstrate esophageal varices failed. Catheterized urine specimens at the time of admission showed the presence of a trace of albumin and 10 to 15 erythrocytes and occasional coarse granular casts per high-power field. Blood cultures were sterile.

The diabetes was readily controlled with dietary measures and supplementary insulin therapy. On the 3rd hospital day, the patient developed fever and pyuria. Urine cultures made 2 days later showed *Escherichia coli*. During the next few weeks, there appeared multiple decubiti, otitis media and endophthalmitis of the left eye, which finally required enucleation. The patient failed progressively, and died on the 38th hospital day.

Autopsy (14 hours post mortem).^{*} In addition to the anticipated urinary-tract, aural and skin infections, the following positive findings were observed.

Culture of the heart's blood showed *Esch. coli*. The liver weighed 1900 gm. and showed parenchymal-cell destruction, many gas bubbles and large clumps of bacilli. There was a comparatively slight neutrophilic reaction. The vertebral bone marrow showed a slight decrease in the number of fat cells, apparently because of a moderate hyperplasia of the red-cell elements, with large numbers of normoblasts and a fair number of megaloblasts. Although there were many mature polymorphonuclear cells, only occasional myelocytes were seen. The normal architecture of the lymph nodes was obscured by marked vascular engorgement and the complete absence of germinal centers. The sinuses were dilated and filled with erythrocytes, lymphocytes and monocytes; some of the last were large and contained phagocytized red cells. The pulp consisted of mature lymphocytes, was extremely vascular, and contained hemosiderin deposits. The spleen was enlarged, weighing 675 gm. On the surface, there was a white, firm, fibrotic area measuring 2.5 by 8.0 cm., interpreted as an old infarct. The normal architecture was indistinct, and the widely dilated sinusoids contained clumps of bacilli. The pulp was composed mostly of many polymorphonuclear cells, large mononuclear cells, erythrocytes and plasma cells. There were also occasional large phagocytes containing red blood cells.

Sections through the articulating surfaces of the patella and femur of one knee joint showed fibrous-tissue ankylosis, destruction of the articular cartilage and its replacement by dense fibrous tissue. Partial obliteration of the joint cavity had taken place, with the formation of smaller cavities lined by a thin layer of synovial cells. The synovial tissues exhibited slight lymphocytic infiltration and contained large pigment-filled phagocytes. The remaining cartilage was chiefly fibrous. The subchondral plate was interrupted in some places, and in many of these areas, the proliferating fibrous tissue had invaded the subchondral marrow spaces. Below the femoral articular surface, there was a large island of degenerating cartilage surrounded by bone trabeculae. A similar island of cartilage was found buried in the patella. All the bony structures showed moderate atrophy. The articular

changes described were those of late and relatively inactive rheumatoid arthritis.

The anatomic diagnoses were as follows: rheumatoid arthritis, generalized; septicemia (*Esch. coli*); otitis media, bilateral, acute; mastoiditis, bilateral; pleuritis, chronic fibrous; pulmonary tuberculosis, right apical, healed; pulmonary infarcts, right lower lobe, with healing; bronchopneumonia; hepatitis, acute, with necrosis; splenomegaly (nonspecific); splenic infarct, healed; pyelonephritis, bilateral, acute and chronic; cystitis, acute; and lymphadenitis, chronic nonspecific.

Although the post-mortem findings in this case indicated sepsis as the chief cause of many of the changes observed, it should be emphasized that the triad of rheumatoid arthritis, splenomegaly and leukopenia was present before clinical evidence of urinary sepsis was obtained.

Except for the terminal septicemia, this case was similar to those described by Felty. The clinical course was characteristic of rheumatoid arthritis, a diagnosis that was readily confirmed by histologic examination. Were the splenomegaly and persistent leukopenia expressions of the same disease or of a concurrent malady? It seems reasonable to assume that the leukopenia was a manifestation of rheumatoid arthritis. However, since splenomegaly is not uncommon in patients with chronic pyelonephritis,² the changes in the spleen may have been due, at least in part, to the pyelonephritis, which obviously antedated the clinical evidence of its presence.

The following are a few brief case histories that illustrate even more clearly that the simultaneous occurrence of rheumatoid arthritis and one of a number of diseases may produce a clinical picture like that described by Felty.

CASE 2. Miss C. W. (M.G.H. 20050), a 40-year-old woman, entered the hospital in February, 1940, because of gastric symptoms. A large gastric ulcer was demonstrated by x-ray examination. The patient readily became symptom free when placed on an ulcer regime. She stated that she had suffered from a severe progressive arthritis for 8 years. Further examination and studies revealed, in addition to the crippling rheumatoid arthritis, a slight generalized lymphadenopathy, a splenomegaly, a persistent leukopenia (white-cell counts varying from 3800 to 4000) and a mild hypochromic anemia, characteristic findings that some have termed Felty's syndrome. It was soon established that the splenomegaly and leukopenia were secondary to hepatic disease caused by cinchophen ingestion 6 years previously. In March, 1941, the patient died from generalized peritonitis following perforation of the gastric ulcer.

Autopsy. Examination confirmed the suspected cause of death and proved the presence of a healed acute yellow atrophy of the liver, chronic congestive splenomegaly with fibrosis, and rheumatoid arthritis.

CASE 3. Mrs. F. B. (M.G.H. 326626), a 67-year-old woman, was first seen in 1933. She had had moderately severe arthritis since 1931. When examined, she showed

^{*}We are indebted to Drs. Granville A. Bennett and Tracy B. Mallory for the report of the pathological findings.

the clinical picture and roentgenographic findings of fairly widespread rheumatoid arthritis. The spleen was readily palpable, and a leukopenia averaging about 3500 and a moderate hypochromic anemia were present. That these clinical findings were due to more than rheumatoid arthritis was suggested in 1934, when the patient expired suddenly because of a massive hematemesis.

Unfortunately, permission for a post mortem examination was not obtained. It was therefore impossible to exclude cirrhosis of the liver with esophageal varices as the cause not only of the fatal hemorrhage but also of the splenomegaly and leukopenia.

CASE 4 Mrs E S (MGH 32491), a 22 year-old woman, presented herself in December, 1940, because of apparent rheumatoid arthritis of 18 months' duration. Splenomegaly, moderate normochromic anemia, slight leukopenia and generalized lymphadenopathy were present. Further search revealed that the splenomegaly and anemia were of at least 11 years' duration, having been noted while the patient was under observation for rheumatic heart disease. Subsequent investigation established the diagnosis of familial hemolytic anemia, and splenectomy was successfully performed.

CASE 5 Mrs F K (MGH 338331), a 32 year old woman, presented the picture of rheumatoid arthritis: generalized adenopathy, splenomegaly, leukopenia and slight hypochromic anemia when first seen. However at subsequent examination, 4 years later, the spleen was no longer palpable and the leukopenia had vanished, and yet the arthritis had progressed somewhat in severity.

In view of these illuminating personal experiences, it seemed worth while to review the literature since 1924 to determine whether the reported cases corresponded to those described by Felty or represented rheumatoid arthritis in association with another disease.

It hardly seems just to attribute the origin of the confusing eponym, "Felty's syndrome," to the observer who first drew attention to this triad. Felty¹ clearly indicated that splenomegaly and leukopenia were known to occur in patients with arthritis but believed it unusual for all three to occur together. Although he stated that "one is more or less forced to the conclusion that the syndrome is a distinct clinical entity, of which the outstanding symptoms are those related to the joints, and the outstanding signs are the enlarged spleen and the blood picture," he did not imply that the articular disturbance was a segregated or unusual joint disease, and he carefully considered the necessity for the elimination of other concurrent pathologic lesions.

The origin of the term, 'Felty's syndrome,' must be directly attributed to Hanrahan and Miller,³ who so classified their case in 1932. Their patient, in addition to the triad of rheumatoid arthritis, splenomegaly and leukopenia, complained of belching and upper abdominal pain. The findings of hepatomegaly, urobilinuria, melena and anemia of the macrocytic type strongly

suggest the existence of an accompanying disease, such as cirrhosis of the liver, although histologic examination of the spleen after its removal revealed nothing specific.

Another illustration of possible hepatic disease occurring in a patient with articular manifestations and giving a clinical picture resembling Felty's cases was reported by Craven⁴ in 1934. This patient also had hepatomegaly and evidence of liver damage as measured by the bromsulfalein test of liver function. Sections of the spleen removed from this case were essentially the same as those reported by Hanrahan and Miller.³

Chronic gouty arthritis can on occasions clinically simulate rheumatoid arthritis.⁵ In the case reported by Fitz,⁶ a history of sudden recurring attacks of "rheumatism" eventually involving most of the joints, an elevated blood uric acid level and roentgenographic changes in certain of the smaller joints suggest that this patient may have had gouty arthritis. It is interesting to note von Jaksch's⁷ case report in 1908 of "arthritis urica" associated with splenomegaly and leukopenia, in which necropsy grossly confirmed the diagnosis of gouty arthritis. Unfortunately, no microscopic findings were reported.

In 1936, Reich⁸ reported a case of Felty's syndrome in which the white cell counts were 7200 and 5300 and in which the joints are not mentioned. In this twenty one year old man with a history of "rheumatism" at the age of six and with an aortic diastolic murmur, fever, night sweats and eventual death, the possibility of subacute bacterial endocarditis or active rheumatic fever was not excluded.

It is interesting that some observers not only have accepted this syndrome as an entity but also have essayed a search for its specific etiology. Singer and Levy⁹ considered this group a special form of sepsis lenta, believing *Streptococcus viridans* to be the causative agent. Unfortunately, their cases presented too many complicating factors to be clearly defined. *Str. viridans* was isolated from the blood of their first case, and the course of the patient's illness was consistent with subacute bacterial endocarditis with fever, generalized petechiae, anemia and, finally, cardiac failure. At autopsy, however, the heart valves were normal, and no source of the bacteremia was found. Their second patient ran a more acute course, with a severe pancytopenia, and the bacteriologic and post mortem findings were similar to those described in the first case.

From the case report by Williams¹⁰ in 1936, one cannot be sure of the exact type of joint disease, the picture being consistent with either a specific infectious or a rheumatoid arthritis. Unfortunately,

the autopsy was restricted to the chest and abdomen, so that the post-mortem diagnosis of hypertrophic arthritis was based on examination of the spine. Williams believed the mechanism responsible for the syndrome to be a primary blood dyscrasia, with secondary articular involvement. From the clinical description given, one may consider it a case of malignant neutropenia, with an associated arthritis of unknown type. This was borne out by bone-marrow studies revealing hyperplasia and maturation arrest of the neutrophilic series.

Curtis and Pollard¹¹ concluded that so-called "Felty's syndrome" was merely a chance variant of ordinary rheumatoid arthritis, since calf-muscle biopsies from 4 patients with rheumatoid arthritis showed a similar picture to those taken from 4 patients with rheumatoid arthritis associated with splenomegaly and leukopenia and from 4 with splenomegaly and leukocytosis. We believe that the relation of muscle histology to joint disease is not sufficiently established to permit conclusions to be drawn. It should also be pointed out that 2 cases in the group reported by these authors had too many complicating features to be acceptable as unequivocally similar to Felty's cases, and that the spleen in another showed amyloid deposits in the follicles.

Diffuse chronic septic splenitis and healed and caseating tubercles in the lung were found at autopsy in the case described by Price and Schoenfeld¹² in 1934. This raises the question of differentiating pulmonary tuberculosis from rheumatoid arthritis as the cause for the splenomegaly in this patient, who appeared clinically to fall into the category under discussion.

Collins's¹³ conclusion that the clinical picture of the arthritis in his 2 cases did not differ from that of rheumatoid arthritis seems warranted. Pathological verification was not obtained.

Lack of adequate studies, before and after death, has been one of the primary difficulties encountered in the classification of cases reported as Felty's syndrome. However, the most exhaustive studies may fail to reveal the exact diagnosis. This was strikingly shown by Steinbrocker and Sesit¹⁴ in their description of a patient who corresponded clinically to Felty's cases. Varied and complete studies, including two lymph-node biopsies, were nonrevealing, and yet histologic study of the spleen after death showed Hodgkin's disease associated with terminal miliary tubercles. The joints were not examined.

It is readily evident that 11 of 14 cases reported in the literature as examples of Felty's syndrome strongly suggest the possibility that the unassociated accompanying disease was responsible for the

splenomegaly and leukopenia. As has been previously pointed out, the pitfalls encountered when this term is used indiscriminately are many. They are due, in great measure, to failure to exclude the existence of some concurrent disease responsible for the enlarged spleen and the leukopenia, as well as failure to realize that splenomegaly and leukopenia may be manifestations of rheumatoid arthritis.

The occurrence of splenomegaly and adenopathy in rheumatoid arthritis was first mentioned in 1896 by Chauffard and Ramond¹⁵ in adults, and in 1897 by Still¹⁶ in children. Since then, diverse figures for the incidence of splenomegaly have appeared: 6 per cent by Waterhouse,¹⁷ 8 per cent by Freund,¹⁸ 10 to 15 per cent by Dawson,¹⁹ 21 per cent by Coates and Delicati²⁰ and 23 per cent by McCrae.²¹ The frequency of lymphadenopathy in this disease has been variously reported as follows: Freund,¹⁸ 19 per cent; Coates and Delicati,²⁰ 53 per cent; Waterhouse,¹⁷ 96 per cent; and others who give no definite figures. These reported differences are probably due to varying assiduity in the search for lymph nodes and differences in criteria for denoting enlargement.

Although slight or moderate grades of leukopenia are not unusual in rheumatoid arthritis, severe neutropenia is rare.²² According to Collins,¹³ whose criteria for the upper limits of a definitely pathologic leukopenia are a white-cell count of 2000 or a neutrophil count of 1000, leukopenia occurs in less than 0.5 per cent of the cases. Incidentally, less than half the cases designated as Felty's syndrome fall within this strict definition. In our unselected series of 293 cases of rheumatoid arthritis, we have observed splenomegaly in 7 per cent, lymphadenopathy in 31 per cent and leukopenia consistently under 5000 in 1 per cent.

In view of these findings, there seems to be no need to assume that any combination of splenomegaly, adenopathy or leukopenia with rheumatoid arthritis represents a new pathologic entity. However, from the figures given, the triad of arthritis, splenomegaly and leukopenia is encountered very rarely. For this reason, numerous concurrent pathologic entities that may cause splenomegaly or leukopenia, or both, in patients with rheumatoid arthritis must be borne in mind. From our experience, the commoner maladies to be searched for are chronic liver disease (cirrhosis or healed acute yellow atrophy), pernicious anemia, leukemia, granulocytopenia, hemolytic anemia, amyloid disease, malignant lymphoma and various acute and chronic infections. In addition, lupus erythematosus disseminatus, dermatomyositis and periarteritis nodosa may present some or all of the features of arthritis, splenomegaly and

leukopenia, and must be considered in the differential diagnosis. We are fully aware of the bizarre and often unrecognizable picture presented by some of these conditions. It is a common experience that the condition may defy diagnosis until the truth is revealed at autopsy.

The evolution of the definition of the clinical entity, rheumatoid arthritis, has been beset with too many confusing variations and the introduction of new terms to encourage their continuance. In Case 1, the articular disorder was obviously rheumatoid arthritis; the leukopenia was presumably a manifestation of the same disease. However, the splenomegaly, as noted above, may be attributed, at least in part, to the chronic pyelonephritis. Our experience and that of others show how often another disorder may be responsible for the splenomegaly and leukopenia observed in patients with rheumatoid arthritis. We therefore believe that the term "Felty's syndrome," which implies a separate pathologic entity, has no reasonable foundation and should be discarded. It is far more important to realize that rheumatoid arthritis is a generalized disease that may affect with varying frequency the lymph nodes, spleen, bone marrow and many other tissues besides the articular structures.

SUMMARY

The clinical record and autopsy findings of a patient whose pathologic picture was similar to the cases described by Felty are presented, with evidence demonstrating the articular disorder to be rheumatoid arthritis. The leukopenia was presumably a manifestation of the same pathologic process, whereas the splenomegaly may have resulted from the arthritis, the chronic pyelonephritis, or both.

The incidence of leukopenia and splenomegaly in association with rheumatoid arthritis, as noted in our clinical experience and in the literature, is enumerated. It is obvious that this triad as an expression of rheumatoid arthritis is but rarely en-

countered. In fact, we have been unable to find any pathologically verified case in the literature or in our own clinical material in which an extraneous cause of the splenomegaly and the leukopenia can be definitely eliminated.

The inadvisability of using the term, "Felty's syndrome," is pointed out. In the rare case in which an extraneous cause of splenomegaly and leukopenia can be eliminated, one should employ the more accurate name, "rheumatoid arthritis," with associated splenomegaly and leukopenia.

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URINARY TYPHOID CARRIERS*

Report of a Case

WESTON T. BUDDINGTON, M.D.,† AND B. BARRETT GILMAN, M.D.‡

BOSTON

THE pyogenic faculty of the typhoid bacillus and the surgical complications of typhoid fever have been the subjects of medical reports and debate for many years. In 1898, Keen¹ published a study based on the analysis of 900 recorded cases in which he discussed the suppurative lesions caused by typhoid bacilli in nearly every organ of the body, including units of the gastrointestinal and genitourinary tracts. These two systems play the leading roles in the carrier state that is considered directly responsible for nearly half the cases of typhoid fever.

Just how frequently one of these systems becomes permanently involved is difficult to say; the bacteriology is a moot point in many of the cases reported in the literature. The records in Massachusetts² from 1937 to 1941 inclusive reveal that there were 405 cases of typhoid fever during that period. The patients were all followed very carefully, and 16 were found to be carriers, 1 being a urinary carrier. This is a much smaller proportion than that found in many other series, possibly because in Massachusetts a person is not classified as a carrier until he is proved to harbor the organism five or more months after his initial infection, and he is not placed on the carrier list until a year has elapsed. This rule avoids the inclusion of patients who excrete the organisms longer than usual during their convalescence. Addition of a name to the permanent carrier list excludes the patient from any occupation that involves the handling of food.

The persistent focus of typhoid infection that is responsible for the carrier state is centered in the gall bladder in most cases. Garbat,³ in his excellent monograph, presents evidence that "liver carriers," that is, carriers with chronic infection in the hepatic ducts or liver tissue, as well as "true intestinal carriers," do occur. Undoubtedly, these types are extremely rare.

Dehler⁴ is credited with being the first to suggest surgical treatment of the carrier state; his article was published in 1907. Since then, many patients have been subjected to surgery for this reason, the great majority for drainage or re-

moval of an infected gall bladder. These operations should not be undertaken unless a duodenal drainage has been done and the culture of the bile found to be positive for *Eberthella typhosa*. The reason for this, of course, is to rule out liver and intestinal carriers. With this precaution, excellent results from the surgical approach may be expected. Over 30 cases in Massachusetts have thus been operated on during a period of several years, with complete success in all but 1. This failure may have been due to a blind pocket of infection in the cystic duct that was not completely removed at the level of its junction with the common duct, or to retained calculi in one of these structures.

Although urinary carriers are far less commonly encountered than fecal carriers, their potential danger to the community is individually greater. This is due to the infectiousness of the excreta (as high as 43,000,000 organisms per cubic centimeter have been recorded³), to the frequency of urination, and to the carelessness in the disposal of urine that seems quite innocuous. Considering that bacilluria in this disease is often found, it is surprising that permanent urinary carriers are not commoner. Garbat³ estimates that 49 per cent of patients present organisms in their urine during convalescence, and believes that such organisms originate in the upper urinary tract in most cases. Of these cases of bacilluria, about 2.5 per cent remain positive for two or three months after the fever has subsided, presumably owing to the presence of renal areas of focal necrosis that discharge bacilli into the excretory passages of the kidney. A small number of this last group become the chronic urinary typhoid carriers, and may thus remain a menace to the health of the community for many years.

In most of the recorded cases of urinary-tract involvement, the carrier state has not received particular mention or emphasis, operation having been undertaken on ordinary surgical grounds for the drainage or removal of infected tissues. Whether the renal damage in such cases is a result of the typhoid infection, or whether the infection has seized on an organ already weakened by previous or concurrent disease, is a question still to be answered. Probably, both conditions occur, but present-day evidence favors the theory

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From the Urological Service, Carney Hospital, and the Division of Communicable Diseases, Massachusetts Department of Public Health.

†Assistant urologist, Carney Hospital.

‡Formerly, epidemiologist, Division of Communicable Diseases, Massachusetts Department of Public Health (Dr. Gilman died on May 31, 1941).

that the typhoid bacillus is generally the secondary invader. The value to the public health of the discovery of these urinary carriers is obvious, but one often fails to recognize the great importance to the individual of determining the reason for his condition. Where is chronic infection of the gall bladder with the typhoid bacillus weakens or destroys no vital organ, a persistent typhoid bacilluria implies upper urinary tract infection, and many of these cases have serious renal lesions.⁵⁻⁸ Thorough urologic study and appropriate treatment may well serve to correct both the disease and the carrier state, as in the following case.

CASE REPORT

The patient (C H 41515), a 37-year-old truck driver became ill in August, 1939, and was admitted to his local hospital the following month with the provisional diagnosis of typhoid fever. It was found that he had been living in a household with a previously discovered carrier, and it was assumed that he had acquired his infection from this source through the medium of food or water. Little could be learned of his clinical course except that he suffered from headache, abdominal cramps and persistent fever ranging between 100 and 103°F. Laboratory study revealed a positive Widal test and two negative stool cultures. Examination of the urine carried out the day after admission, showed innumerable pus cells in the sediment; no other investigation was made. The nurses' notes state that at no time did the patient seem very ill, and after an apparently uneventful recovery he was discharged on October 28, 1939, about 6 weeks after admission.

Because cultures of mixed stool and urine specimens were still positive for typhoid bacteria a year later the patient's name was added to the carrier list of the Massachusetts Department of Public Health, and further study was begun. Specimens of bile obtained through a duodenal tube at this time (November 1, 1940) were negative, but a urine culture was positive, and the Department of Public Health, with the consent of the patient, arranged for complete urologic examination.

Little could be learned from the record, for there was no history of any serious illness or injury or of any complaint referable to the urinary tract, except for an occasional indefinite pain in the back. There had been no dysuria, hematuria, increased frequency or nocturia. Physical examination showed the patient to be a thin but otherwise healthy man with no significant defects. Neither kidney was palpable and there was no costo-vertebral tenderness. The external genitals were normal. Rectal examination revealed a small, firm, benign prostate, uniform in consistence. There was no thickening in either seminal vesicle region.

Cystoscopy revealed an irritable bladder, which tolerated no more than 120 cc of fluid. However, the mucosa, ureteral orifices, trigone and internal sphincter margin were normal in appearance. A No 5 Fr catheter was passed easily along the right ureter for 30 cm, and a clear, rhythmic drip was obtained, which later became blood-tinged. On the left side, neither a No 5 nor a No 4 Fr catheter could be advanced beyond 22 cm. Phenolphthalein given intravenously appeared in 2 minutes on the right side, and a 10 minute collection showed an excretion of 9 per cent of the dye in 20 cc of urine. No determination of function could be made on the left,

since only a few drops of urine were obtained. The bladder urine contained many pus cells, free and in clumps and on culture *E. typhosa* was recovered. Urine from the right kidney was normal and showed no growth, whereas that from the left kidney was positive on culture for typhoid bacilli. A retrograde pyelogram revealed normal excretory passages on the right, but none of the opaque solution passed up the ureter on the left side beyond the point of obstruction, where an elliptical calculus was lodged (Fig 1). In the left renal area, there was a



FIGURE 1 Retrograde Pyelogram

The right side is normal but there is a large calculus at the tip of the ureteral catheter on the left

group of three small stones in the region of the lower pole of the kidney. Intravenous pyelograms again demonstrated good function on the right side, but there was very faint and delayed excretion of the dye on the left.

Two problems were thus presented: a badly damaged left kidney, as a result of ureteral obstruction and infection and a typhoid carrier state probably associated with this condition. After careful consideration of the medical and social aspects of the case, operation was decided on.

The patient re-entered the hospital on February 4, 1941. The interval history gave no new information. Physical examination showed no additional changes as compared with the earlier investigation, and an x-ray film showed the ureteral calculus to be in essentially the same position. Because of the rather long interval since the cystoscopic study the bladder inspection was repeated, with exploration of the left ureter and intravenous injection of indigo carmine. The bladder was normal, and the dye appeared at the right ureteral orifice in good concentration in 4½ minutes. No dye appeared on the left side during the period of the observation, which was extended to 50 minutes. A No 4 Fr ureteral catheter was blocked at

essentially the same level as before, and there was no drip of urine. Another attempt at a left retrograde pyelogram was unsuccessful; there was still complete obstruction of the ureter by the stone. Culture of the bladder urine again showed *E. typhosa*. The white-cell and red-cell counts were 5900 and 4,300,000 respectively; the hemoglobin was 95 per cent; and the differential count showed 70 per cent polymorphonuclears, 28 per cent lymphocytes, and 2 per cent basophils. The blood Wassermann reaction was negative, as was a blood culture and a Widal test. Blood sugar, calcium, phosphorus and uric acid determinations were all normal.

Operation was performed on February 6. A left lumbar incision was made, with preservation of the 11th and 12th intercostal nerves. When the renal fossa was entered, a large, soft kidney was found, with surprisingly few inflammatory adhesions. The renal parenchyma was extremely thin as a result of the severe hydronephrosis. The calculi noted in the x-ray films could be palpated in the lower calyx and upper ureter. Because of the extreme destructive changes present in the kidney and because of the serious infection known to exist, it was decided that nephrectomy should be performed. This was easily accomplished after a small vascular pedicle was isolated. A few centimeters of the upper ureter, including the region of the impacted calculus, was removed with the specimen.

The pathological report was as follows:

The specimen consists of a previously partially sectioned kidney weighing 120 gm. It measures 13 by 6 by 3 cm. There is an attached portion of the ureter, 8 cm. in length. When the incision is continued in the usual manner and the kidney divided into halves, the pelvis and calyces are greatly dilated, so that there remains only a narrow rim of renal parenchyma, measuring 3 mm. around the periphery. The pelvis and calyces are lined by glistening, gray, finely granular mucosa. Three stones are seen, the largest 0.4 cm. and having prongs on the surface. The ureter communicates with the pelvis and is markedly dilated, for the most part up to 2 cm. in circumference, but narrows suddenly to almost pinpoint size at the level where it is tied (Fig. 2).

Microscopic diagnosis: chronic pyelonephritis, hydronephrosis, hydroureter and nephrolithiasis. Cultures taken from the renal cavity and from the ureteral calculus showed *E. typhosa*.

The patient made an uneventful convalescence. A small amount of secondary wound infection at the posterior angle of the incision responded to drainage and the application of heat; culture of the pus failed to grow typhoid bacilli. The patient was discharged in good condition on March 2. He was seen 1 month and 2 months later in the Out-Patient Department, at which time he reported that he was feeling well and had no urinary complaints. Examination of the urine showed it to be normal except for 0 to 3 pus cells per high-power field in the sediment. The incision was dry and well healed.

Cultures of the bladder urine taken on the following dates were negative for typhoid infection: February 19 and 22; March 1, 10, 17, 24 and 27; May 5, 24 and 26;



FIGURE 2. Gross Specimen Sectioned Longitudinally.

Note the thin rim of parenchyma at the periphery and the dilated pelvis and calyces.

and July 5. The patient's name was removed from the carrier list shortly after the last negative culture.

SUMMARY

The typhoid-carrier state in most cases is due to residual chronic infection in the gall bladder. In a small but important percentage of cases, the focus of infection is in the urinary tract.

All persons in this latter group should have complete urologic investigation, for many of them have serious renal lesions.

An illustrative case is reported: surgical treatment corrected the carrier state and removed a dangerously infected kidney.

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FURTHER EXPERIENCE WITH ELECTRIC-SHOCK THERAPY IN MENTAL DISEASE*

ABRAHAM MYLERTON, M.D.†

BOSTON

THE use of electric-shock therapy in the psychoses has become routine in many of the hospitals for mental diseases in the United States and in the private practice of many psychiatrists. An accumulated literature makes it possible to give with a greater degree of certainty the indications for the use of this method. These may be considered under two headings: injuries and risks, and accumulated experience regarding the type of case in which a favorable result may be anticipated and that in which little of value is to be expected.

Method of Treatment

Of the 123 patients in this series, 74 were treated by what I¹ have previously described as the "out-patient method"—that is, the patients reported at a place fitted out in hospital fashion with nurses and a physician in attendance, were given the shock treatment and, usually within one or two hours, went home. In a few cases, the patient was too disturbed after the treatment for the return home to be practical, and was transferred to a hospital for mental diseases to complete the series of treatments. In 2 other cases, injury precluded the return home, and transfer was made to in-patient care. In general, it can be stated that out-patient care of many psychiatric cases is very useful. It often makes commitment unnecessary, and although it must not in any sense be informal or without proper safeguard, it is, on the whole, as safe as in-patient care.

Injuries and Risks of Method

No fatalities have been recorded since the early days of the treatment. There is considerable difference of opinion concerning the pathologic cerebral changes produced. The Italian workers, Cerletti and Bini,² and Kalinowsky et al.^{3,4} found no serious neuropathologic changes in dogs. Smith and his co-workers^{5,6} found punctate hemorrhages in cats.

The fact that memory is definitely impaired for a variable period indicates that some organic change is produced. In the vast majority of cases, this impairment of memory disappears to a point where it is no longer discernible to the patient or

to those around him. In other cases, there is some subjective difficulty in memory for several months, although not to the point of incapacity or disability. Since the best clinical results are often obtained when the patient is shocked into amnesia, it may very well be that one of the conditions of recovery from a psychosis by the shock treatments depends on the temporary brain damage, probably most frequently swelling and possibly punctate hemorrhages. Only by speculation can one postulate a relevant change in any specific brain area or function.

Since the treatment has been in use in the United States for over three years and since cases have been observed for that period, it can now safely be stated that no severe damage of consequential type is done to the brain. Certainly, subdural and subarachnoid hemorrhages are not recorded in human beings. No neurologic signs have been noted after twenty-four hours in any of the cases that I have studied, and there is no record of such changes in the experience of other workers.

When the nature of the conditions treated and the suffering and doubtful prognosis are taken into account, it can on the whole be stated that the risk of brain damage by electric shock is fundamentally inconsequential when compared with the conditions treated: involutional melancholia, marked and severe depression, schizophrenia and the paranoid psychoses. Certainly, in an era in which hypothermia, hyperthermia, lobotomy and lobectomy are being carried out for the treatment of mental diseases, electric shock is, relatively speaking, a mild approach.

Injuries have been greatly reduced. The commonest complication is fracture of a vertebral transverse process. In this series of 123 cases, only 1 such fracture occurred. It was not disabling, and the patient recovered spontaneously and without orthopedic care. A fairly common type of injury in elderly people is either the precipitation of subdeltoid bursitis or its aggravation, if already present. Three such cases occurred in this series, and all responded to physiotherapy. The most unusual case of injury in the group was that of a fifty-year-old woman mentally sick for years with a chronic depressive state, presenting a moderate amount of osteoporosis common at her age and

*From the Division of Psychiatric Research, Boston State Hospital.
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†Professor emeritus of neurology, Tufts College Medical School; clinical professor of psychiatry, Harvard Medical School; director of research, Boston State Hospital.

an anemia of considerable degree, who had a fracture of both acetabulums, with displacement of the heads of the femurs into the pelvis. Since this patient is still under treatment, the physical outcome cannot be stated. Mentally, she became clear after one electric shock and has remained so. It may be of value, consequently, to study the amount of calcium in the blood and to make a careful study of the bony structure of the pelvis in certain cases, although in the case mentioned above there was no basis for such a study from the history of the patient.

Electrocardiographic changes have been described as occurring within the first twenty-four hours after shock treatment. The recording returns to normal, however, within the same twenty-four hours. This may mean that the contraindications for treatment are severe arteriosclerosis, cardiac disease and very marked circulatory involvement. My own experience does not indicate any great degree of danger even with existing cardiac disease, although decompensation and severe arterial disturbances are certainly sufficient reasons not to undertake the treatment.

There are mental diseases, however, in which aggravated damage to the heart and circulation follows from the nature of the psychosis itself, as when an elderly patient suffering from cardiac and arterial disease becomes so intensely agitated and restless because of his profound emotional state that his circulation and the integrity of his heart become disturbed. Under such circumstances, I have weighed the risk of treatment against the risk of the disease and have given the treatment on the basis that the risk was warranted. There are 4 such cases in my records, of which I cite 2. One patient, a man with severe cardiac disease, frequent attacks of angina pectoris and one previous attack of coronary thrombosis, who presented the picture of a very severe agitated depression, recovered promptly after eight electric-shock treatments and has remained well; electrocardiographic studies made before and after treatment showed no change in the condition of his heart due to the electric shock. The other patient, a woman with myocarditis that warranted the use of digitalis in maintenance dosage, received seven shocks without any apparent damage to the heart or circulation, although her mental condition was only temporarily relieved. It can safely be stated that an ordinary degree of cardiac and vascular change need not be a contraindication if the psychosis warrants treatment.

Treatment was also given to a woman with a severe case of diabetes requiring 60 units of insulin a day. She received nine shock treatments over a considerable time, with no evidence of

change in the diabetic state and with marked improvement in the mental state. There was a slight temporary change in the color of the urine after each treatment.

One patient with pernicious anemia, with a red-cell count of slightly over 2,000,000 and a hemoglobin somewhat under 50 per cent and with other evidence of vitamin deficiency, was treated (four shocks) with good results and without any effect on the pernicious anemia except perhaps in the direction of improvement, since her appetite returned and she ate a greater amount and a greater variety of food.

One case of Paget's disease in a man of over seventy was also treated (five shocks) by this method, without damage to the bony structure.

I believe that the technic used plays some part in the low rate of injury and that the physiology of electric-shock treatment is a significant factor in explaining the fact that moderate organic disease of the heart and other organs of the body is not a contraindication to the treatment. I have been very careful in the use of sandbags and a firm bed to support the back. Pillows have routinely been placed under the knees, so that it is impossible for the patient to get his feet down to the table and thus to put an extra strain on the back and other parts. Great care has been taken to prevent the shoulders from rotating outward and upward. A gag, made of felt and carefully inserted and watched during the procedure, has prevented any dislocations of the jaw; in fact, none have occurred for over a year.

The fact that with proper precautions few serious injuries take place is confirmed by most other reports. For example, the Boston State Hospital, which has given a large number of electric-shock treatments in the past year, has an exceptionally fine record so far as injuries are concerned. The method, therefore, may be declared safe. This, I repeat, does not mean that it is to be used indiscriminately, or without proper hospital conditions.

Unlike Metrazol, the electric-shock treatment causes a fall in the blood pressure. For a very short time, the patient is pulseless, but within a few seconds the pulse returns. There is less cyanosis than with Metrazol. There is no sweating. There is very little evidence of vasomotor disturbance. The gastrointestinal tract does not seem disturbed. There is rarely any nausea or vomiting, and there is no interference with the function of the bladder.

It has been recorded that there is a possibility of spontaneous epileptic attacks following shock treatment. The literature on this point is very scanty, and the evidence of such a result is not at

all conclusive. In fact, Kalinowsky et al.^{3,4} believe that electric shock offers a method of treatment for epilepsy. I have seen only 1 case in which there were epileptic attacks of minor type following treatment. This occurred in a fifty nine year-old woman with arteriosclerosis. After the treatment had been concluded, she had on successive days two short attacks of unconsciousness closely resembling those seen in arteriosclerosis, with some convulsive twitchings of the face and arms. There was no evidence of subdural or subarachnoid hemorrhage. In my opinion, the danger of setting up epilepsy by electric shock can be discounted.

Indications for Treatment

In considering the type of case that responds to this treatment, one must remember that psychiat-

only approximations to roughly delineated clinical syndromes, and disappointment in the result or even the unexpected good result cannot at present be explained.

In general, one may say that the electric-shock treatment is of little value in the fully developed schizophrenic state, with splitting of personality, hallucinations, delusions of reference, and negativistic or catatonic reactions—more especially, when the condition has lasted for years. Cases that are diagnosed as early schizophrenia sometimes do remarkably well, but the question of differential diagnosis is essential in an interpretation of the results. Thus, in one of my cases that had lasted for two years and had been diagnosed as schizophrenia, very good results were obtained with four shocks, and the recovery has lasted for six months. However, a study of the family

TABLE 1 *Results of Electric-Shock Treatment of Mental Disorders*

DIAGNOSIS	TOTAL NO OF CASES	METHOD OF TREATMENT		NO IM- PROVE- MENT	SLIGHT IM- PROVE- MENT	RESULTS				RECOV- ERY
		IN HOSPITAL	OUT- PATIENT			TEMPO- RARY IMPROVE- MENT	MOD- ERATE IMPROVE- MENT	MARKED IMPROVE- MENT	NO RE- SULT	
Manic depressive psychosis										
Manic phase	7	1	2	2	0	1	0	0	0	0
Depressive phase	20	9	11	1	0	2	7	0	6	4
Depression										
Recurrent depression	7	1	6	0	1	0	2	2	2	2
Depressive psychosis	6	4	2	0	0	0	2	1	1	3
Chronic depressive state	12	1	11	3	0	0	6	2	1	1
Agitated depression	3	2	1	1	0	0	0	1	1	1
Depressive state	7	3	4	0	0	0	3	0	4	0
Unclassified depression	2	0	2	0	0	0	2	0	0	0
Involuntary melancholia	9	3	6	0	1	0	2	0	0	6
Senile melancholia	3	1	2	0	0	1	1	1	0	0
Anhedonia (unrealistic syndrome)	3	2	1	0	0	1	1	1	0	0
Schizophrenia	23	18	5	8	3	6	4	2	0	0
Paranoid state	4	2	2	4	0	0	0	0	0	0
Unclassified psychosis	2	1	1	0	0	1	0	0	1	0
Obsessive compulsive state	6	1	5	2	0	2	2	0	0	0
Psychopathic personality	2	0	2	1	0	0	1	0	0	0
Psychoneurosis and anxiety state	11	0	11	5	0	2	4	0	0	0
Totals	123	49	74	27	5	16	37	16	22	

ric diagnosis has not reached the stage where it is possible to discriminate with any exactness between the various types of so-called "functional psychoses," such as schizophrenia, manic depressive psychosis, involuntal melancholia and the unclassified depressions, and the various severe neuroses. There is an abundant literature concerning this difficulty. Thus, a case diagnosed as schizophrenia by one clinician may be diagnosed by another as a marked depressive retreat. A patient who presents a neurosis at one stage of his mental disease may later show schizophrenia or some form of the depressive psychoses. Moreover, depressive psychoses may be substantially different, even though with the present inadequate methods of diagnosis and study they show a similar general clinical picture. Therefore, all statements regarding the value of this treatment can be regarded as

history shows cases of manic-depressive psychosis, and the study of the past history of the patient herself is not at all conclusive of schizophrenia. It has been stated by some writers that schizophrenic patients need a large number of shocks for improvement or recovery. In 3 of this series of cases, more than fifty shocks were given, with no fundamental improvement in these well-marked schizophrenic states, the average number of shocks given in the other diagnostic groups being about seven, or even less. Conduct improvement often takes place, and temporary improvement is remarkably frequent. Unfortunately, in the vast majority of cases of clearly differentiated schizophrenia, the patient slips back into his previous state.

Electric shock is also of little advantage in the paranoid psychoses. Some cases with paranoid

coloring, that is, patients whose underlying state is fundamentally depressive, do very well. The patient believes himself to be persecuted, but when this delusion is analyzed, it is found that he is being persecuted because of his derelictions or for his good rather than because of the gratuitous hostility and malevolence of others.

In the obsessive-compulsive neuroses I have obtained no permanent benefit by the use of this method. The literature, on the whole, bears out this statement.

The involutional melancholias, with clearly marked depression, great agitation, anxiety, feelings of unreality or nihilistic delusions, on the whole do well with this form of treatment. This is the unanimous conclusion in the literature, and is borne out by my own experience (Table 1). One sometimes sees improvement in these cases after one, two or three treatments. The sequence of events seems to be that sleep is first restored, and that, as the memory becomes somewhat impaired, the delusions disappear and a genial and jovial mood replaces the melancholia. In a large number of cases, this improvement persists. There are relapses, however, and the treatment can by no means be called a cure. Nevertheless the improvement is so prompt and lasts in so many cases for so long that this can be called the best approach to the symptom complex at present.

Experience with senile melancholia in cases occurring after the age of seventy is insufficient for any conclusions. In 2 patients whom I have treated, there was marked temporary improvement, but no subsequent permanent gain.

The result of treatment of the depressive phase of the manic-depressive psychosis is similar to that of the individual melancholias. There is immediate improvement with treatment, usually after the third or fourth shock. The attack is frequently remarkably shortened in duration and intensity, and even where there is some slipping back, it does not generally reach the former level of despair and death seeking. It must be stated at this point, however, that when the attacks are frequent,—that is, when the cycle repeats itself every few months or even more frequently,—electric shock does not seem to me to be warranted. Part of the result of the treatment of the depressive states is the appearance of a mild euphoria. A manic state often supervenes, usually of less intensity than the depression, and often without any definite handicap to the patient. When the manic attack may appear at any time, however, it seems inadvisable to administer the electric shock. This statement is made because the manic attack itself does not seem in any fundamental way to be improved by shock therapy. Conduct improve-

ment takes place, and a very wild patient is more easily managed. Within a week or two after the treatment has been terminated, the patient becomes as manic as ever. I have therefore discontinued the electric-shock treatment in the manic states, except when its use lessens the strain of the arduous care of the patient.

Very good results are obtained in cases of chronic depression, such as I⁷ have elsewhere described as the "anhedonic state," and one cannot explain these cases on the basis of coincidence. In several such cases in my records, patients have remained anhedonic for several years and without improvement, despite the type of treatment used. Following a few shock treatments, the mood alters *pari passu* with the number of shocks given and the appearance of some impairment of memory. In some cases, a moderate exhilaration appears and persists for a long time, but is not troublesome.

Electric shock has not given marked relief in the neuroses, especially the anxiety neuroses that are marked by paresthesias occurring under excitement, with a sense of marked visceral disturbance, either of heart, head or other parts, and with marked fear localized as phobias or as diffuse agitation and anxiety. In these cases, the patient, usually being noncommittable, refuses to continue the treatment after a few shocks are given.

At this point, it is safe to say that the statement made in the literature that there is no fear of the treatment is not correct; there is less than with Metrazol shock, and often enough the individual treatment is not at all remembered. In the relatively sane patients, the whole matter of repairing to a hospital, of becoming unconscious and of a period of agitation and loss of memory afterward becomes linked up with the idea of treatment, and a definite association fear of the treatment develops. In the markedly psychotic cases, no such fear seems to be experienced.

I have not been able to treat in any consecutive manner such conditions as neurasthenia and hysteria. In a few chronic cases, I have attempted to carry out the treatment, but the patients have themselves put an end to this by refusing to undergo more than one, two or three shocks.

Summarizing the indications, one may say that when a disturbance in affect or mood is the main psychopathologic feature, electric-shock treatment has a very reasonable prospect of bringing about marked improvement, recovery or, at the worst, remission. This includes the depressive states, the anhedonic states and the cases of involutional melancholia. This is not true, however, of the affective disturbance called the manic phase of manic-depressive psychosis. In functional or nonestab-

lished pathologic mental diseases, such as schizophrenia, the paranoid psychoses, the obsessive compulsive states and the anxiety neuroses, the results have not been particularly gratifying. Temporary improvement is common, permanent or durable improvement is not frequent. When the differential diagnosis is in doubt,—that is, when it is difficult to differentiate a mental disturbance of the schizophrenic type and one belonging on the whole to the mood and affect disorders,—it is justifiable to use this method, since on the whole no harm is done and the prognosis is so poor as to warrant anything that offers hope.

In Table 1, the diagnoses include a great variety of depressions that some other workers might perhaps classify with the manic depressive states. The difference is that certain classic phases of the manic depressive state did not occur in this group of patients. Most of them were not retarded, a good many had no delusions of any kind, and some were definitely not psychotic in the technical sense. The main feature in common was an affect disturbance of a depressive nature.

It is necessary to define the term 'anhedonia unreality syndrome'. By this is meant a state in which there is complete lack of desire and satisfaction for the visceral enjoyments, such as eating, sleeping and sexual relations, as well as a failure in energy and the capacity to work, linked with a feeling of unreality sometimes related to the outer world and sometimes including the patient himself. It is possible that this group of cases is also allied to the manic-depressive state. The patients are not insane in the usual sense and have good insight.

By the term 'slight improvement' is meant conduct alteration and a lesser expression of the psychosis. 'Temporary improvement' goes farther: the patient seems quite well for a short time—two or three weeks to two or three months. 'Moderate improvement' means that the patient shows conduct improvement and a general lessening of psychotic and mental symptoms directly following the treatment and maintained indefinitely. By 'much improvement' is meant an extension of this classification further, difficult to make quantitatively but representing a clinical impression. 'Recovery' means that the particular attack disappears and, so far as can be seen, there are no mental signs whatever.

SUMMARY

The injuries resulting from electric shock therapy, and the risks encountered, are discussed. The indications and contraindications in various neuroses and psychoses are considered. Experience with this form of therapy in 123 cases of mental disorders is presented.

475 Commonwealth Avenue

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CLINICAL NOTES

ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS ASSOCIATED WITH FINGER LESIONS RESEMBLING LUPUS PERNIO*

REPORT OF A CASE

JOHN G. DOWNING, M.D.,†
AND SALVATORE J. MESSINA, M.D.

BOSTON

THE following case is of interest because the initial lesions were seen on the tips of the fingers, when a diagnosis of lupus pernio was made. However, the typical butterfly lesion of the face soon appeared, and the patient complained of abdominal pain, nausea and vomiting, and muscular and joint pains; these symptoms clinched the diagnosis of lupus erythematosus disseminatus.

CASE REPORT

G. C., a 15-year-old girl, was first seen at the Medical Clinic of the Out-Patient Department, Boston City Hospital, in December, 1938, complaining of loss of energy, general malaise and stiffness and soreness of the fingers of both hands for the previous few weeks. The patient was referred to the Skin Clinic in January, 1939. Physical examination revealed erythematous infiltrations on the flexor and lateral aspects of the fingers. These areas were rather tender. The hands were cold and clammy. A diagnosis of lupus pernio was made.

During the next week, ulcerative changes were observed on the skin of the fingers. The volar surface showed several round to oval lesions 2 or 3 mm. in diameter, with smooth raised red edges and central scaling depressions. Physical examination was negative except for the fingers. Two weeks later, a faint butterfly lesion on the face was evident. X-ray examination of the hands, feet and lungs was negative. Tuberculin tests in dilutions of 1:10,000 and 1:1000 were negative. The blood Hinton reaction was positive. Biopsy showed hyperkeratosis and no atrophy of the epidermis, acanthosis, and elongation and matting of the rete pegs. The corium showed lymphocytic and perivascular infiltrations; there was no evidence of true tubercles. At this time, weekly injections of 1 cc. of bismuth were begun. After eight such treatments, there was a marked improvement, the central depressions of the lesions of the fingers becoming less evident and the erythematous color fading to normal skin color. A blood Hinton reaction was doubtful, but both Kahn and Wassermann reactions were negative.

The patient was admitted to the hospital in June. Three days before admission, she had noted fever, without chills. In the mornings, there was mild nausea, and vomiting occurred soon after eating. There was mild, cramplike abdominal pain.

Physical examination revealed an erythematous patch,

3 cm. in diameter, above the bridge of the nose, herpetic lesions about the nose and mouth, and hemorrhagic oval lesions, 5 mm. in diameter, on the hard palate. The lungs were clear, and examination of the heart revealed no murmurs. The abdomen showed generalized and rebound tenderness. The liver and spleen were palpable at the costal margins. The volar surface of the fingers showed reddish-purple, oval, depressed atrophic patches, 5 to 10 mm. in diameter. The hospital stay was characterized by an elevated temperature (103°F.), which gradually fell to normal in 2 weeks. The daily urines showed albumin except for two specimens. The white-cell count, which was 2300 on admission, gradually rose to normal by the 7th hospital day. The patient became asymptomatic at the end of the 2nd week, and was discharged on the 23rd day with a diagnosis of lupus erythematosus disseminatus.

The patient returned to the Skin Clinic and was again given 1 cc. of bismuth weekly. In November, 1939, she was seen at the Vascular Clinic, and a diagnosis of Raynaud's disease was made. In May, 1940, she was exposed to the sun and developed the typical butterfly patch of lupus erythematosus on the face. Two weeks later, she began to have soreness of the throat and morning bleeding from the mouth, gums and throat, accompanied by a weak and feverish feeling. Hospitalization was advised.

The patient was readmitted to the hospital in June. The face showed a red, slightly raised eruption confluent except at the periphery, where there were isolated papules, not indurated, blanching on pressure, with prominent follicles on the involved area, and a roughly butterfly distribution involving the nose and cheeks and extending up to the ears and the sides of the face and over both eyebrows. There were slightly indurated papules becoming confluent over the upper lip, involving both the skin and the mucous membrane. Multiple small circinate red lesions 1 to 3 mm. in diameter were seen over the gums, hard palate and gum margins. The thorax and abdomen showed lesions like those on the fingers. The tongue was coated and fissured. The teeth were carious. The tonsils were moderately enlarged but showed no redness; the hair showed evidence of alopecia. The pupils were slightly irregular but reacted to light and distance, and in the right fundus, a fading flame-shaped hemorrhage was observed; pea-sized axillary and inguinal nodes and bean-sized tonsillar nodes were palpated; the trachea was in the midline. The lungs were clear to percussion and auscultation. The heart was enlarged, rapid, regular and overactive, and the pulmonic second sound was greater than the aortic; there were blowing systolic murmurs at the apex and in the pulmonic area. The abdomen was flat, with no spasm or tenderness. The liver was felt 3 cm. below the costal margin; the edges were sharp and soft. The spleen was 1 cm. below the costal margin in the left lateral position. The reflexes were physiologic. The blood pressure was 104/64.

Daily examinations of the urine showed a specific gravity of 1.010 to 1.020, an acid reaction, and slight traces to traces of albumin in all but three specimens. The sediment contained a few to many white blood cells, usually in clumps, very rare red blood cells on only one occasion and coarse granular casts just before death.

The hemoglobin, which was 75 per cent on admission, fell to 45 per cent 3 days before death. The red-cell count was 3,800,000 on admission and 2,700,000 before death. The white-cell count varied between 5200 and 5000; differential counts on admission showed 78 per cent polymorpho-

*From the Department of Dermatology and Syphilology of the Boston City Hospital and of Tufts College Medical School.
†Visiting physician for diseases of the skin, Boston City Hospital.

nuclears, 17 per cent lymphocytes, 1 per cent monocytes and 5 per cent young forms. The blood Hinton reaction was positive on three occasions and doubtful twice. The blood Wassermann and Kahn reactions were negative on two occasions. The nonprotein nitrogen was 41 mg per 100 cc. on admission, rising to 60 mg 4 days before death. The total protein, which was 6.6 gm per 100 cc on admission, was 6.5 gm 10 days later. The albumin globulin ratio was 3.9:2.6. The blood sodium was 133 mg per 100 cc., 2 weeks later, it was 130 mg. The chlorides were 571 mg per 100 cc. The potassium was not recorded. The calcium was 8.5 and the phosphorus 5.1 mg per 100 cc. The phosphatase was 3.2 Bodinsky units. Four blood cultures revealed no growth, but one culture showed streptococcus, subsequent cultures were negative. The phenolsulfonphthalein was 44 per cent in 2 minutes. The Widal test was negative. The clotting time was 15 and the bleeding time 3 minutes. The mean corpuscular volume was 93 per cent. The prothrombin time was 31 and the coagulation time 13 minutes. The icteric index was 7, the urobilinogen 1.8 mg per 100 cc., and the sedimentation rate 17. Three stool examinations revealed negative guaiac reactions.

A chest plate revealed clear lung fields.

An electrocardiogram showed normal sinus rhythm, a PR interval of 0.16 second and a QS complex of 0.06 second, T_1 was upright, T_2 was flat, and T_3 and T_4 were inverted. The left ventricular predominance was interpreted as showing myocardial disease.

The patient was hospitalized for 26 days, during which she steadily failed. The temperature varied from 100 to 102°F daily. There was mild generalized abdominal pain, with nausea and intractable vomiting. The lesion on the face faded somewhat, but the mucous membrane lesion progressed and became confluent. Frequent nosebleeds and hemorrhages from the gums were present. At the end of the 3rd week, the patient was having severe gastro-intestinal symptoms, vomiting and abdominal pain, hyperpyrexia (104°F) and increasing asthenia, she had lost 10 pounds since admission. The blood pressure rose somewhat with administration of 10 mg desoxycorticosterone daily. On the 26th hospital day, the patient went into peripheral vascular collapse, and death followed in a few minutes. No autopsy was performed.

This case of acute disseminated lupus erythematosus is reported because of the unusual sequence of symptoms and physical signs shown by the patient, and because the opportunity to follow a patient from what is deemed clinically a benign symptom complex to a later fatal disease is rare. The uncommon but confusing laboratory findings, in view of state laws demanding serologic examinations before marriage, should be of interest to all physicians. This case shows that the dermatologic eruption was only a physical sign of a serious systemic disease that was further complicated by abdominal symptoms suggesting the need of surgical interference.

520 Commonwealth Avenue

THE USE OF IODINE TO DELINEATE A SAFETY ZONE IN THE RECTUM*

DAVID C. DITMORE, MD†

BOSTON

WHEN or by whom iodine was first used as a vital tissue stain, I do not know. However, the fact that certain cells take up the dye more readily than others was first brought to the attention of the medical profession by Schiller‡ in his work on the early diagnosis of cancer of the cervix. I have found that the affinity of the tissues just above the pectinate line of the rectum for the simple tincture or the compound solution of iodine varies so decidedly that the use of either is of great assistance when one is working in this area. In fact, there is definitely outlined the distal border of a portion of the rectal wall that, since it has little tendency to bleed and does not respond to painful stimuli, may be termed the "safety zone." The existence of this zone is so manifest and the test to locate it so simple that I hesitate to claim anything new in it, but general knowledge concerning the phenomenon is lacking, I am quite sure, and for that reason I shall describe the technic of its demonstration.

After a swab of cotton on an applicator is dipped into the iodine, it is withdrawn and held momentarily against the mouth of the container so that any excess fluid may escape. The area to be investigated, already isolated in the anoscope, is then prodded gently with the iodine soaked swab. If no change in color appears, the anoscope is slowly withdrawn with the free hand, while prodding with the iodine swab is continued. At some point above the pectinate line, the tissue will be seen to become deep black.

The stained area follows no uniform pattern. In some cases, there may be a continuous or broken band no more than 2 or 3 mm in width tracing the upper border of the pectinate line. On the other hand, the stained area may be from 15 to 20 mm in width, with the upper border very irregular. Regardless of the extent of the heavily stained tissue, the operator may, by confining himself to the zone immediately proximal to it, proceed with minor surgery without fear of complications such as excessive bleeding, pain and external edema. He must, of course, observe ordinary surgical technic.

*From the Department of Proctology, Boston University School of Medicine and the Massachusetts Memorial Hospital.
†Instructor in proctology, Boston University School of Medicine; proctologist at Massachusetts Memorial Hospital.

‡Schiller, W. Zur klinischen Frühagnose des Portalkarzinoms. *Zentralblatt f. Gynäk.* 52:1885-1892, 1928.

I am not qualified to discuss the mechanism of this staining reaction. Much has been written about it. Everyone seems to agree that columnar cells do not take the stain, whereas cuboidal or squamous cells with a high content of glycogen stain readily. I have never seen it mentioned that highly vascular tissue stains more readily than avascular tissue, but this seems to be true, at least in the lower rectum.

The practical values of this test are many. For example, in the safety zone, biopsy, insertion of a hypodermic needle and removal of small benign tumors are simple procedures. Proximal or distal

to that area, the same operation may cause much unhappiness both to the physician and patient.

CONCLUSIONS

Variations in the affinity for iodine of normal tissue cells of the anorectum are as striking as those described by Schiller in his work on carcinoma of the cervix.

Taking advantage of this property, one can roughly locate the pectinate line and establish a safety zone in which minor surgical procedures may be carried out.

7 Bay State Road

MEDICAL PROGRESS

RADIATION THERAPY

RICHARD DRESSER, M.D.*

BOSTON

THE recent advances that have been made by physicists and engineers in the construction of x-ray generators have placed at the disposal of the radiotherapist a wide variety of wave lengths in intensities greater than were dreamed of a decade ago. It is natural that some confusion regarding the relative merits of these wave lengths should exist, not only in the minds of practitioners but also among radiologists themselves. Although the clinical results of radiation treatment can be evaluated only after years of painstaking observation, the intelligent application of roentgen rays or radium rays should be based on a knowledge of their physical properties as well as their biologic effects. The physics of radiology has been set forth simply and concisely in a recent treatise by Robertson.¹ A review of this work should help the practitioner to understand some of the problems that confront the specialist in radiation therapy.

Radium is an element that is continually disintegrating. In the process of decay, three types of energy are given off—alpha, beta and gamma rays. If the rays from a radium source are submitted to the action of a strong magnet, the alpha rays are deflected in one direction and the beta rays in the opposite direction; the gamma rays are unaffected by the magnetic field. The alpha rays are actual particles of matter bearing a

positive electric charge. The beta rays, which likewise particles of matter, carry a negative charge. The gamma rays have no mass, but are electromagnetic vibrations. The alpha rays may be disregarded in therapeutic work, since they have little penetrating power and are filtered out by the wall of the radium container. The beta rays have considerable penetrating power and are frequently used, particularly in the field of dermatology, for the treatment of superficial lesions. The gamma rays are the most important of the radium rays. They have essentially the same properties as x-rays but are much shorter and more penetrating than the x-rays in common use. Recently, it has been possible to produce x-rays that are as short or even shorter than the gamma rays of radium.

Radium element is most commonly used in the form of one of its salts, either the sulfate or chloride. Metal tubes are filled with the salt and sealed off at either end. Frequently, the tube has an eye at one end and a point at the other, forming what is known as a radium needle. A special type of applicator may be inserted into a tumor mass and withdrawn, after the required dose has been given, by means of a string threaded through the eye. It is often desirable in radiation treatment to exclude the beta rays, leaving only penetrating gamma radiation. This is done by interposition of a metal screen or filter between the radium source and the tissue irradiated. It is now common practice to make the wall of the container of some metal of sufficient density and thickness to remove all beta radiation without adding screening. The commonest filters, listed in

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*Radiologist, New England Medical Center, and Free Hospital for Women, Brookline; assistant radiologist, Massachusetts General Hospital.

of their effectiveness, are platinum, gold, lead, silver and brass. Radium dosage, when the element is used, is expressed in milligram hours: that is, the number of milligrams employed multiplied by the time of application in hours. Thus, 10 mg. applied for five hours would give a dose of 50 mg. hr. Likewise, 25 mg. applied for two hours would give the same dose.

Another form in which radium is used is known as radium emanation or radon. Radon is a gas that is given off from radium and, by means of a specially designed pumping and purifying system, can be collected in capillary tubes of glass or gold. The development of the so-called "radium emanation plant" was due in a large measure to the researches of the late William Duane, professor of biophysics at Harvard University. After the capillary tubes have been filled with radon, they are cut into small sections, which are automatically sealed in the process of cutting. These capillary sections are known as radon seeds or implants. They emit both beta and gamma radiation; however, if a gold capillary is used, a large percentage of the beta radiation is filtered out. The great difference between radium element and radon is that the former takes one thousand six hundred and ninety years to degenerate to half strength, whereas the latter becomes inactive for practical purposes in about thirty days. One makes the application of radon seeds by placing the implant in a suitable trocar. The trocar is pushed into the neoplasm to the desired depth, and a stylet then pushes out the seed. When the trocar is withdrawn, the seed remains in the tumor. Radon dosage is expressed in millicurie hours, 1 mc. hr. being equal in intensity to 1 mg. hr. Each millicurie of radon delivers, in its decay period of thirty days, 130 mc. hr. Thus, if a seed of 2-mc. strength is inserted, the total dose is figured as 260 mc. hr. Radon seeds may be employed to advantage in locations where it would be difficult to insert or to hold element needles in place,—for example, in a carcinoma of the tonsil.

Credit for the development of an x-ray tube whose output can be accurately controlled is due Coolidge, former director of the research laboratories of the General Electric Company. When a wire is heated to incandescence in a vacuum tube, small negative particles of electricity are liberated about the wire. This is known as ionization by heat, or the Edison effect. By application of a high-voltage current to the tube, these ions may be drawn away from the wire filament and made to move at high velocity toward the target or anode of the tube. The impact of the electrons against the anode, which is usually a block of tungsten, results in x-ray production. It has already been noted that the commonly employed

roentgen rays are identical with the gamma rays of radium except in wave length.

The physical properties of x-rays may be considered from the standpoint of intensity or quantity, and of quality. If the amount of current applied to the tube is varied, the amount of x-ray emitted varies in direct proportion. If, however, the voltage of the current is varied, the x-ray output varies approximately as the square. More simply, if the voltage on the tube is increased from 100,000 to 200,000, all other factors remaining constant, the x-ray production will be quadrupled. X-rays and light rays follow the same law in regard to distance: that is, the intensity varies inversely as the square of the distance. For example, if one assumes that it takes ten minutes to administer a certain x-ray dose at a distance of 25 cm. from the source of radiation to the skin of the patient, and if this distance is doubled,—that is, increased to 50 cm.,—not one half but one fourth the amount of radiation reaches the patient. It then takes not ten but forty minutes to give the same x-ray dose.

To explain variations in the quality of radiation, one may draw an analogy between a beam of x-rays and a beam of sunlight. When sunlight is passed through a glass prism, the well-known spectrum results, because of a breaking up of the beam into its constituent wave lengths. The violet band at one end of the spectrum represents the shortest visible wave lengths, whereas the red band at the opposite end represents the longest visible wave lengths. By passing an x-ray beam through a prism, let us say of rock salt, one can obtain an analogous spectrum. This, of course, is not visible, but the various bands can be recorded by photographic and other methods. It will be found that the beam is not homogeneous but is composed of a variety of wave lengths. By raising of the voltage on the x-ray tube, shorter wave lengths are added to the beam; there is more "violet" radiation if one uses the analogy of the light spectrum. If the potential is increased to between 2,000,000 and 3,000,000 volts, the short wave lengths of the beam are identical with the shortest gamma rays of radium. If one wishes to employ only the short wave lengths of an x-ray beam, the longer rays must in some manner be excluded. This is done by the use of filters, as in radium work. The common filters are lead, copper, a combination of tin and copper, and aluminum. Lead is used in filtering rays produced at 1,000,000 volts and upward. Copper, or tin and copper are used for rays of 200,000 to 500,000 volts, and aluminum for rays produced at 100,000 to 150,000 volts.

X-ray dosage is commonly expressed either in

terms of the visible effects on the skin or by a physical measurement of intensity known as the roentgen unit (r). If a certain amount of radiation is given to the skin, a mild redness appears in ten days to three weeks after exposure. The amount of radiation necessary to produce this effect is called the "erythema dose." A slightly smaller amount causes epilation of a hairy area, and is known as the "epilation dose." X-rays passing through the air cause an electrical upset in the atoms that is termed "ionization." The amount of ionization is directly proportional to the intensity of the x-ray beam. The roentgen unit is based on a physical measurement of the amount of ionization occurring in 1 cc. of air. It has become the internationally accepted standard of x-ray dosage.

The treatment of superficial lesions concerns chiefly x-rays of long wave length — that is, the relatively nonpenetrating variety. Many benign dermatologic conditions, together with cancerous or precancerous lesions of the skin, can be adequately handled by rays produced at not more than 100,000 volts. Any good radiographic machine equipped with the proper tube is entirely adequate to handle such cases. If, however, a lesion is situated at some distance below the surface, it is obviously impractical to attempt treatment with 100,000-volt x-rays whose energy is largely dissipated within the first 2 or 3 cm. of tissue. One must resort to shorter wave lengths, which necessitate high voltage for their generation. A second factor of equal significance in the treatment of deep-seated lesions concerns the inverse square law. For example, a carcinoma of the body of the uterus is to be irradiated; this organ is located approximately at the center of the pelvis, about 10 cm. from the surface in the average patient. If the source of radiation were placed 10 cm. from the patient's skin and the absorption of energy in the intervening tissue entirely disregarded, only 25 per cent of the dose delivered to the surface would reach the tumor. If the source were moved to 50 cm. from the patient, it would take twenty-five times as long to give the dose to the skin, but the tumor would receive 69 per cent of the surface radiation. This is a purely theoretical consideration, and in actual practice, the figure of 69 per cent would be considerably reduced by tissue absorption. Radium would afford an ideal source of energy for external application if it could be obtained in sufficient quantity. However, when the amount of radium ordinarily available is placed at sufficient distance from the patient to deliver an adequate depth dose, the time of application becomes so long that the method is not practical. The commonly employed "deep

therapy" x-ray unit, which operates at about 200,000 volts, can be used at distances of 50 to 80 cm. without undue prolongation of the treatment time. The amount of radiation delivered below the surface with this type of therapeutic apparatus is greater than that obtainable from the usual radium application. Radium is chiefly valuable in the treatment of readily accessible, fairly well localized growths, in which it can be used by direct application or by implantation. Frequently a combination of x-ray and radium therapy is advisable, one treatment supplementing the other.²

Roentgen rays generated at potentials considerably in excess of 200,000 volts are now available and are known as "supervoltage rays." It has been possible to produce these rays in tremendous intensities with wave lengths as short and penetrating as the gamma rays of radium. The treatment time at a distance of 100 cm. or more is relatively short. It should be emphasized that there is nothing new in the quality of supervoltage x-rays. The advocate of radium therapy becomes, unwittingly or otherwise, an advocate of supervoltage roentgen therapy, since the two types of radiation can now be made identical.

As the wave length of an x-ray beam is decreased, — that is, as the voltage and filtration are increased, — certain physical and biologic changes have been observed: there is an increase in the amount of radiation delivered below the surface (depth dose); there is a lessening of skin reaction (it takes more roentgen units to produce an erythema); the size of the portal of entry has less effect on depth dose; and there is less scattered radiation. These facts have been established beyond question.³⁻⁵ A review of the conflicting observations on the therapeutic value of supervoltage x-ray would, at present, be confusing. However, an intense source of radiant energy of a quality equivalent to the gamma rays of radium is certain to occupy a major place in the armamentarium of the radiotherapist.

The method of application of radium or roentgen rays varies in some degree with the training and experience of the radiologist. A small, accessible growth may often be successfully treated by a single intensive dose. The radiation necrosis resulting from such therapy will heal satisfactorily provided the area irradiated is not too large. If the disease is extensive or deeply situated, the so-called "divided dose" is usually employed. This consists of relatively small amounts of radiation administered daily, or perhaps at longer intervals, with an extension of the treatment series over a period of days, weeks or even months.⁶ Presumably, neoplastic cells have a slower rate of recovery from the damaging effects of radiation than nor-

mal cells, and it is on this basis that the divided dose technic has been established. The aim is to build up a total intensity that will be lethal to cancer tissue, but from which the normal structures included in the field of radiation will recover.

A reasonably accurate prognosis following radiation therapy is not only difficult but frequently impossible. The pathologist can be of considerable help, but one must still rely to a large degree on the method of trial and error. Warren⁷ states

While it may be said that, as a rule, less differentiated tumors are more radiosensitive, this is not completely correct. Indeed, our knowledge of the response of various tumors to irradiation rests largely on empirical grounds. It should be mentioned in passing that while histologic grading of malignancy is of some assistance

in estimating radiosensitivity, many tumors of the higher grades are radioresistant, and some of the lower grades radiosensitive. Even with tumors of the same histologic type there may be variation in response, and even in the most resistant types an exceptional case may respond well to radiation therapy.

129 Bay State Road

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28371

PRESENTATION OF CASE

First admission. A fifty-nine-year-old Portuguese unemployed cabinet-maker was admitted to the hospital because of hematuria, followed by pain in the back and a chill.

The patient was in good health until ten days before entry, when he began to pass bright-red blood in the urine. The urine then became a persistent, uniform dark brown. Dull backache developed, about equally on both sides. The pain was unrelated to respiration and was not relieved by strapping. The day before entry, the patient had a shaking chill followed by profuse perspiration. There was no nocturia, dysuria or other urinary symptom.

Thirty years before admission, the patient had gonorrhea, characterized by an acute urethral discharge. This was cured after several months' treatment. A few years later, some bright-red blood appeared in the urine without antecedent manipulations, and the urine became dark colored. The patient took some pills, and the urine again became normal. At no time were there any symptoms of stricture. No instruments were ever passed. Nine years before entry, the patient began to have burning epigastric distress coming on just before meals and usually relieved by food. Acid and gaseous eructations were associated. An "ulcer" was demonstrated by roentgenogram, and medical treatment was instituted. After two years, the symptoms previously noted became severer, with stabbing pain, vomiting and tarry stools. Roentgenograms taken in this clinic and in another metropolitan hospital showed an active duodenal ulcer. Ultimately, subtotal gastric resection, with posterior Polya anastomosis, was performed in this hospital. The postoperative course was uneventful, and the patient remained symptom free in the four years preceding his re-entry for different complaints.

On admission, the patient appeared frail, thin and ill. The heart was of normal size, with distant sounds. The lungs were normal. There was well-defined tenderness in the left costovertebral angle, without spasm or palpable mass. The abdomen was normal except for the scar of the previous laparotomy. The prostate was one and

a half times normal size and rubbery, without nodules.

The blood pressure was 130 systolic, 80 diastolic. The temperature was 100°F., the pulse 80, and the respirations 18.

Examination of the blood showed a red-cell count of 4,400,000 with 70 per cent hemoglobin, and a white-cell count of 9600 with 69 per cent polymorphonuclears, 22 per cent small lymphocytes, 7 per cent monocytes and 2 per cent eosinophils. The blood Hinton reaction was negative. The non-protein nitrogen was 33 mg. per 100 cc. The urine showed a ++ test for albumin, with many red and white cells in the sediment.

An intravenous pyelogram showed prompt excretion of the dye. The upper calyces of the left kidney were slightly dilated, but the corresponding pelvis was not visualized. The right renal pelvis and calyces were normal. The kidney outlines were not visible. The spine showed lateral curvature and rarefaction of the bones, without evidence of metastatic lesions. There was a large filling defect in the base of the bladder suggesting an enlarged prostate, and the bladder showed trabeculation.

A second intravenous pyelogram failed to confirm a filling defect in the left pelvis. A flat roentgenogram of the abdomen showed normal kidney shadows.

Following dilatation of a stricture of the urethra, cystoscopy was performed. The bladder was markedly trabeculated, but no stones or tumor was evident. The median lobe of the prostate was hypertrophied. Urine cultures taken from each ureter grew colon bacilli, and were negative for tuberculosis on guinea-pig injection.

A left retrograde pyelogram showed definite dilatation of the upper calyces, but was otherwise unsatisfactory owing to movement of the patient. On the sixteenth hospital day, the patient was discharged, pending the report on the urine cultures.

Second admission (three weeks later). Four days after discharge from the hospital, the patient noticed recurrence of slight ache in the back and flanks. Four days later, severe pain appeared in both left and right flanks, associated with chills and two episodes of gross hematuria. The flank pain became increasingly severe. There was constant malaise.

On re-examination, the patient appeared essentially as before. Costovertebral tenderness was marked on the left and but slight on the right.

The temperature was 102°F., the pulse 90, and the respirations 25.

Laboratory data were much as before. The white-cell count was 28,400.

The day after entry, ureteral catheterization was attempted, but resistance was encountered high at the left ureter. The next day, the patient was very sensitive over the costovertebral angles, but complained of pain over the mastoid process. There were no physical signs of parotitis. The patient was given sulfathiazole, with a prompt fall

lobulated. No barium could be brought into the cavity from the gastrointestinal tract. The remnant of the stomach was displaced to the right and anteriorly. The splenic flexure of the colon was displaced downward. Smaller, irregular, air-filled spaces lay in the left midabdomen below the large cavity. The midportion of the small intes-



FIGURE 1. *Roentgenogram Showing Large Pocket of Air and Fluid beneath the Dome of the Left Diaphragm.*

in the temperature. An intravenous pyelogram showed no essential changes from earlier examinations. Roentgenograms of the cervical and dorsal spine were essentially negative. After a week and a half, the patient still complained of pain in the neck. Retrograde pyelography of the left kidney was again unsuccessful, owing to ureteral block. A rise in temperature followed the manipulation.

Roentgenograms of the gastrointestinal tract showed a large pocket of air and fluid beneath the dome of the left diaphragm, posteriorly, measuring 7 cm. in diameter (Fig. 1). The lower and medial borders of this cavity were irregularly

une was displaced forward slightly, on the left. On the thirty-second hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM C. QUINBY*: "The urine then became a persistent, uniform dark brown." This has no specific significance except that it means that the blood was shed some time before it appeared. One does not as a rule find a patient passing urine of this type unless there has been precipitation of hemoglobin. The change to brown color has very little clinical significance.

*Clinical professor emeritus of genitourinary surgery, Harvard Medical School, chief, Urological Service, Peter Bent Brigham Hospital.

"Subtotal gastric resection, with posterior Polya anastomosis, was performed in this hospital." That is an operation, as I understand it, in which one reduces the size of the nonacid-producing part of the stomach by a resection of its terminal portion. Nothing is said about the specimen removed at that operation.

I do not know what the term "rubbery" means. It could be anything from sponge rubber to bakelite, I suppose. There were no nodules, and no suggestion that the prostate was carcinomatous.

The hemoglobin and red-cell count were not low for a person said to appear chronically ill. Evidently, the hematuria was no longer severe. The white-cell count was also not suggestive of any severe infection. The renal function seemed normal.

On intravenous pyelography, there was seen some suggestion of dilatation of the upper calyces on the left—the side on which tenderness had been elicited. The pyelogram on the right was normal. "The kidney outlines were not visible." One is interested to know why they were not, but no explanation is given. In a patient who is thin and chronically ill, it should be possible to see the outline of the kidney in a properly exposed film, unless a soft-tissue mass or gas or something of that sort obscures the renal shadow. At a second pyelography, however, the renal shadows appeared normal. At this time also, the "pyelogram failed to confirm a filling defect in the left pelvis." Does this mean that the pelvis appeared normal, or just what does it mean? We are not told.

A cystoscopy was performed; presumably, whatever stricture may have been present was easily dilated, so that the instrument could be passed and therefore had played no part in the patient's difficulties. Nothing much is said about the cystoscopy on this examination except that there was "hypertrophy of the median lobe." Since the prostate was found to be enlarged on re-examination, there must have been some other enlargement than that of the median lobe, for it could not be felt rectally. No statement regarding the urine appears. On the whole, I must regard the prostate as the cause of the patient's difficulties. The left retrograde pyelogram showed dilatation of the upper calyces. Here, again, we have confirmation of the first intravenous pyelogram. The cultures of the urine showed the color change in each kidney.

During the three weeks out of the hospital, the patient did badly, and had more back pain; although this was in evidence on re-examination, it revealed much more tenderness on the left. At this time, his poorer condition

was accentuated by a leukocytosis and fever. At a second cystoscopy, the statement is made that resistance to the passage of the catheter was met "by the left ureter." But this is again indefinite. If the catheter pass 20 or 25 cm., the normal distance being 30 cm.? We do not know. Also, at this nor at the previous cystoscopy was there any mention of bloody urine from either catheter. We do not know whether to assume that the hematuria was from the left or the right side or neither.

Pain over the mastoid process is a queer complaint in this story. I should like to know whether there was any evidence of infection, or whether there was any discharge from the ear. Nothing is said about the mastoid process. They did not x-ray the mastoid process, but they did x-ray the cervical spine, with negative results.

Two further x-ray examinations were made: an endeavor to learn more about the left kidney. The intravenous injection showed nothing new than before, and the retrograde route again showed a blocked ureter. Ten days later he complained of pain in the neck. I do not know what this means. At this time, the bladder was empty of the gastrointestinal tract. A flat roentgenogram showed no pocket of air and fluid beneath the diaphragm. This showed normal kidney x-ray films?

Dr. Larrabee performed a stricture of the ureter. The bladder was seen, but no stones or tumors were seen. The median lobe of the prostate was enlarged. Urine cultures taken from the bladder showed a few colon bacilli, and were negative for tuberculosis on guinea-pig injection. The retrograde pyelogram showed definite dilatation of the upper calyces, but was otherwise normal. Owing to movement of the patient, the pyelogram of the sixteenth hospital day, the patient was discharged, pending the report on the urine cultures.

Second admission (three weeks later). Four days after discharge from the hospital, the patient noticed recurrence of slight ache in the back and flanks. Four days later, severe pain appeared in both left and right flanks, associated with chills and two episodes of gross hematuria. The flank pain became increasingly severe. There was constant malaise.

On re-examination, the patient appeared essentially as before. Costovertebral tenderness was marked on the left and but slight on the right. The temperature was 102°F., the pulse 90, and the respirations 25.

Laboratory data were much as before. The white-cell count was 28,400.

out I think in this case it is safest to go on the evidence of the roentgenologist and at least assume that the cause of the air was not primarily bowel.

We must consider the question of the operation, a resection of the stomach four years previously. In the meantime, the patient was perfectly well. That type of resection is not made as a rule for cancer, which in a duodenal ulcer is not nearly so common, although it does occur, as an ulcer situated on the proximal side of the pylorus—namely, a gastric ulcer. But each of these areas had been removed. It is accordingly very difficult to see how this manifest abscess had anything to do with the previous operation, or how it could have any special connection with the intestine. So, it was on the left side, bearing no relation to septic pylephlebitis or liver abscess.

I thought first of actinomycosis (not very uncommon in the intestine) involving the colon and the rectum, of which there is no evidence. There is no justification for assuming that the prostate contained a tumor of the kidney, or that the abscess was necrotic and secondarily infected.

Could this phenomenon follow a rupture of the kidney? Probably not. The roentgenogram shows no evidence of a rupture. The patient had general peritonitis and sometimes a localized abscess. The area of the abscess seems to be of the type of a carbuncle. The operative outlook was bad.

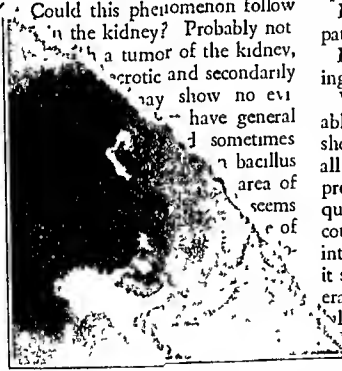


FIGURE 1. Roentgenogram Showing Large Abscess beneath the Dome of the Left Diaphragm.

An intravenous pyelogram showed no essential changes from earlier examinations. Roentgenograms of the cervical and dorsal spine were essentially negative. After a week and a half, the patient still complained of pain in the neck. Retrograde pyelography of the left kidney was again unsuccessful, owing to ureteral block. A rise in temperature followed the manipulation.

Roentgenograms of the gastrointestinal tract showed a large pocket of air and fluid beneath the dome of the left diaphragm, posteriorly, measuring 7 cm. in diameter (Fig. 1). The lower and medial borders of this cavity were irregularly

to the perinephritic tissues. I am thinking especially of the so-called "renal carbuncle." This is about as near as I can come to making a diagnosis: that the patient had a renal carbuncle, which ruptured into the perinephritic tissues, and that an abscess eventually resulted in the production of gas and fluid making it visible on x-ray examination. Of course, that process takes some time, as a rule, and I am surprised, therefore, at the relatively short illness of this patient, but I do not see that this invalidates my diagnosis.

What was the matter with the mastoid process? I have not the remotest idea. What the pain in the neck was due to, I do not know. These things might very easily have been related to a general systemic infection. We are told nothing about blood cultures and given only the story that at some time or other the patient had chills. We are not given his hospital temperature chart. He was operated on, presumably for drainage of this abscess and also for a more accurate diagnosis than it was possible to make before operation.

DR. TRACY B. MALLORY: Here is the chart. The patient did have a fever all the time.

DR. QUINBY: Yes; but this is not a very striking chart.

What happened after the operation, I am not able to say, of course. We are not told that. I should guess that the patient died. I think in all probability he went on to a long suppurative process in the retroperitoneum and upper left quadrant of the abdomen. I do not know, of course, what these air pockets among the small intestines are. If these are related to the abscess, it seems to me that the condition had spread generally throughout the abdomen, and in all probability the operative outlook was bad.

DR. MALLORY: Then your first choice would be a renal carbuncle?

QUINBY: Yes; if you like that term. It is a Staphylococcus aureus infection of the retroperitoneum and may go on to suppuration of the renal substance.

On the third day after the operation, the patient was performing well. It is also occurred to me, and I wondered whether it might not be a carbuncle of the retroperitoneum.

DR. WILLIAM: It is due to the staphylococcus, I should think.

came a persistent fever. The gas was not present all the time. There was a number of x-ray films that do not show the abscess. There may have been secondary infection of the colon bacillus, a very frequent cause of peritonitis. There was a very frequent passing of urine. There was a precipitation of brown color in the urine.

M. CHAPMAN: I should like to ask whether the possibility of perforation of the colon with the catheter at the time the

*Clinical professor of medicine, Harvard Medical School, chief, Urology.

left retrograde pyelogram was done. The history states that the film was unsatisfactory because of motion. The patient was very active. Is that a possible explanation of the subdiaphragmatic abscess on the left? Does such an accident ever occur?

DR. QUINBY: I do not believe the patient suffered perforation of the ureter by the catheter. That might occur on an attempt to pass a catheter in a ureter adherent or obstructed low in its course, but when 20 cm. of catheter has been introduced, there cannot be enough force exerted to perforate a ureter unless the ureter is already necrotic. That is a possibility, but there is no evidence of it here.

DR. CHAPMAN: I thought the pain in the left neck was explainable as referred pain from diaphragmatic irritation.

DR. QUINBY: I suppose one might have pain in the mastoid process from suppuration under the diaphragm, but it must be rare.

DR. MALLORY: We have seen coronary, and I think pleural, pain referred to that area. It is reassuring to hear the urologist tell us it is almost impossible to perforate the ureter.

DR. J. DELLINGER BARNEY: I have never seen it.

DR. QUINBY: Certainly not high perforation; one cannot exert enough force.

DR. MALLORY: Have you any comment, Dr. Robbins?

DR. ROBBINS: Only that the left kidney is displaced downward by this mass, and I should say from the one retrograde pyelogram film that there is pressure on the upper margin of the pelvis.

DR. GEORGE G. SMITH: The only comment I have is that the story does not quite seem to hang together with the picture. So far as the hematuria goes, it would be a possible accompaniment of infection, but it was a rather unusual amount.

DR. QUINBY: An extrarenal mass making pressure on the renal vein will cause hematuria.

CLINICAL DIAGNOSIS

Subdiaphragmatic abscess.

DR. QUINBY'S DIAGNOSIS

Renal carbuncle of left kidney, with perforation into subdiaphragmatic region, forming abscess containing gas.

ANATOMICAL DIAGNOSIS

Hypernephroma of left kidney, containing colon-bacillus abscess.

PATHOLOGICAL DISCUSSION

DR. MALLORY: There was a great deal of difference of opinion and argument on the service

regarding the diagnosis in this case, and eventually, I believe, the patient was transferred from the Urological Service to the Surgical Service on the basis that there was enough chance that the subdiaphragmatic abscess was connected with the gastrointestinal tract to make it wiser to operate from in front rather than from behind.

He was operated on by a general surgeon, and a large tumor mass was found in the kidney area. The mass was removed with some difficulty and proved to be a hypernephroma. In its center was a large cavity in the midst of broken-down and infected tumor tissue, and the gas was all within the hypernephroma. There was no subdiaphragmatic abscess. The patient made an excellent post-operative recovery.

DR. QUINBY: He would not have if the gas had been among the loops of bowel.

CASE 28372

PRESENTATION OF CASE

First admission. A thirteen-year-old schoolboy was first admitted to the hospital because of polyuria and polydipsia.

Two weeks before entry, the patient noticed that he was forced to urinate more frequently than usual, and that he was passing large amounts of urine at each voiding. At the same time, he began to void two or three times each night. He drank at least ten glasses of water a day and seemed hungrier than usual, especially between meals. After several days, he was taken to a physician and found to have sugar in the urine. He was put on a diet and referred to the hospital.

When the patient was two years old, he had a period of "vomiting and malnutrition." At that time, a physician found sugar in the urine. This finding was not followed up. Before the onset of the evident increase in urination, the patient had occasional nocturnal enuresis. Two years before entry, he had scarlet fever, with no symptoms referable to the kidneys. A sister three years younger than the patient had scarlet fever at the age of nine, and was recognized as diabetic at fourteen. Her subsequent course bore a remarkable resemblance to that of the patient. She developed albuminuria after nine years, and retinal hemorrhages and arteriolar narrowing, a blood pressure of 160 systolic, 96 diastolic, edema and a palpable liver after ten years. The patient's father later developed diabetes, hypertension and albuminuria.

On admission, the patient appeared well developed, with evidence of some recent weight loss. The tonsils were enlarged and cryptic, with caseous inclusions. The heart was of normal

size, with a soft systolic murmur at the apex. The abdomen was normal.

The blood pressure was 100 systolic, 65 diastolic. The temperature, pulse and respirations were normal.

Examination of the urine showed 45 per cent sugar, no albumin and rare white cells in the sediment. The blood showed a red cell count of 5,000,000 with 85 per cent hemoglobin, and a white cell count of 5200 with 66 per cent polymorpho nuclears. The blood Wassermann reaction was negative.

The patient was given a special diet, with insulin adjusted to free the urine of sugar. After stabilization, tonsillectomy and adenoidectomy were performed, and he was discharged to the clinic on a maintenance dose of 5 units of insulin a day.

Second admission (ten years later) An acutely inflamed appendix was removed. The patient had continued to be well during this interval, with the insulin varying from 10 to 30 units a day and diet regulation.

Third admission (two years later) The patient, aged twenty-five, had continued in satisfactory health on 40 units of insulin a day. He was readmitted to the hospital because of a cold of three days' duration. The day before re entry, he took an extra 10 units of insulin because of glycosuria, and subsequently suffered a slight insulin reaction.

On examination, the patient appeared restless, and flushed, with congestion of the conjunctivae and of the nasal mucous membranes.

The blood pressure was 128 systolic, 88 diastolic. The temperature was 100.2°F, the pulse 80, and the respirations 20.

The urine showed a trace of sugar but no albumin or abnormal sediment. The red cell count was 3,800,000 with 70 per cent hemoglobin and the white cell count 7000 with 69 per cent polymorphonuclears. The fasting blood sugar was 212 mg per 100 cc on the second hospital day. After two weeks, the patient was discharged on 45 units of protamine insulin a day.

Fourth admission (three and a half years later) The patient continued well except for several insulin reactions that necessitated reduction in daily dosage to 40 units of protamine insulin. Two months before re entry, he changed jobs to do work at irregular night hours. This occasioned difficulty in the adjustment of his meals and insulin. The urine showed sugar in several tests. At about this time, he dropped a heavy weight on his right great toe and later stubbed it. A blister formed near the nail, but soon healed. Five days before re entry, the toe was stubbed again, and became

red in several hours. The next night, the patient had a shaking chill and perspired profusely. He was admitted to the emergency ward of the hospital the next day, where it was found that he had a tender thick callus on the medial aspect of the right great toe, red streaks running up the leg, and tender inguinal lymph nodes. The callus was incised, with release of 2 cc. of pus. The leg was given local heat and elevation. The patient was transferred to the medical ward for readjustment of the insulin dosage.

Examination at this time showed blurring of the disk margin of the right fundus, with marked vascular proliferation over the disk extending into the vitreous. Many small retinal hemorrhages were present. The left eye showed a similar but less advanced picture. The chest was normal. The liver edge was displaced three fingerbreadths below the costal margin on deep respiration. The dorsalis pedis and posterior tibial arteries were palpable. The infection of the right great toe and the accompanying lymphangitis had subsided.

The blood pressure was 130 systolic, 100 diastolic. The temperature, pulse and respirations were normal.

The urine showed a +++ test for albumin in four out of five examinations, traces of sugar, and occasional red and white cells and a few fine granular casts in the sediment. The blood counts were essentially normal. The blood sugar varied from 40 to 120 mg per 100 cc. The blood cholesterol was 229 mg. per 100 cc.

A roentgenogram of the right foot showed a soft tissue swelling of the distal phalanx of the great toe, without evidence of osteomyelitis. The vessels appeared calcified.

Cultures of the urine showed *Staphylococcus aureus* and nonhemolytic streptococci. The patient was discharged sugar free on 40 units of protamine insulin a day to attend to some urgent business.

Fifth admission (four days later). The patient returned for further study. Physical examination and routine laboratory studies were as before. The phenolsulfonephthalein excretion was 60 per cent. Urine concentration tests showed ability to concentrate up to a specific gravity of 1.028. The non-protein nitrogen varied from 29 to 42 mg per 100 cc.

A flat film of the abdomen showed well outlined, slightly enlarged kidneys, with sharp shadows. There was marked calcification of the pelvic arteries. Intravenous pyelograms showed impaired secretion of the dye on the left. Retrograde pyelograms were negative.

No changes were visualized by cystoscopy. Urine from the left kidney showed an occasional white

cell, and gave a moderate growth of colon bacilli. Urine from the right kidney showed 300 red cells per high-power field, with an occasional white cell, and was sterile on culture. Following a moderate reaction to the cystoscopy, the patient was given a course of sulfathiazole. After a week, urine cultures grew nonhemolytic streptococci. After three weeks, the patient again left the hospital for business reasons.

Sixth admission (five days later). The patient returned to the hospital for continuance of studies. Physical examination and routine laboratory studies were essentially as before. Cystoscopy was again performed. The urine obtained from both kidneys was clear. That from the left kidney gave abundant growth of colon bacilli. The phenolsulfonephthalein appearance time was 3 minutes for the left kidney and 4 minutes for the right, with good concentration of the dye on each side. The patient was discharged after a week, on his usual routine.

Seventh admission (one year later). The patient continued to be fairly well, although lacking ambition and strength. He noted that his urine was "cloudy." Three days before entry, there was a sudden onset of sharp pain in the right flank, followed or accompanied by a shaking chill, with a temperature of 101°F. The pain did not radiate, and soon subsided. The night before re-entry, a similar sequence of pain, chill and fever occurred.

Physical examination was as before except for the presence of tenderness in the right flank and costovertebral angle. The pulse, temperature and respirations were normal.

The urine showed a +++ test for albumin, with 10 red cells and 25 white cells per high-power field and with occasional coarse granular casts. Abundant growth of colon bacilli was obtained on culture.

The patient was given sulfathiazole for two weeks. The urine became sterile and cleared except for a few red cells and persistent albuminuria. On discharge, the patient remained on his usual insulin.

Eighth admission (one year later). Three months after discharge, the patient gradually lost central vision in the right eye because of increasing opacity of the vitreous. He continued at work. Five months before re-entry, he began to note edema of the legs and nocturia. The blood pressure was found in the clinic to be 190 systolic, 110 diastolic. Ammonium chloride was prescribed, but was soon discontinued because of indigestion. Gradually, exertional dyspnea appeared, with puffiness of the eyes. A month before re-entry, headaches were noted, centering over the right eye. Following an upper respiratory infection,

generalized aches and pains developed. In the two weeks before re-entry, vision began to fail in the left eye. The patient suffered almost constant severe frontal headaches, vomiting and edema of the eyes and legs. At the time of entry, he was thirty years old.

Examination showed a pale, chronically ill man with edema of the face, sacrum and lower extremities. Vision was limited to finger counting at twelve inches. The heart was at the upper limits of normal size, with sounds of good quality and regular rhythm; the aortic second sound was greater than the pulmonic. The lung fields were clear. The abdomen showed questionable evidence of free fluid. There was moderate tenderness in the right costovertebral angle.

The blood pressure was 210 systolic, 130 diastolic. The temperature, pulse and respiration were normal.

The urine showed a +++ test for albumin, a trace of sugar and a specific gravity of 1.010, with occasional red and white cells and hyaline and granular casts. The red-cell count was 3,400,000 with 11.2 gm. hemoglobin, and the white-cell count 13,200. The nonprotein nitrogen was 45 mg. and the serum protein 4.1 gm. per 100 cc. The carbon dioxide combining power was 23.4 milliequiv. and the chlorides 104.2 milliequiv. per liter. The calcium was 10.6 mg., the phosphorus 4.2 mg., and the phosphatase 4.1 Bodansky units per 100 cc.

Intravenous pyelograms showed no definite excretion of dye in the course of an hour.

The patient did poorly. There was frequent vomiting, and the peripheral edema persisted. A furuncle slowly developed on the right leg. It was poulticed at first, and later incised and drained. The patient was discharged slightly improved after five weeks.

Final admission (two days later). The patient remained in bed at home. At 2 o'clock in the morning of the day of re-entry, he had a brief generalized convulsion. He was then rational for three hours, when he became unresponsive except to painful stimuli, and had frequent generalized convulsions. He had taken the usual dose of 20 units of protamine insulin on the preceding day.

On examination, the skin was hot and dry. The eyeballs were firm and roving. The heart action was rapid and regular, with a scratchy sound heard only during systole and limited to the pulmonic area. The lungs seemed clear. The bladder was distended to two fingerbreadths above the umbilicus. Tendon reflexes were active, with bilateral Babinski plantar responses.

The blood pressure was 260 systolic, 150 diastolic. The temperature was 104°F., the pulse 140, and the respirations 35.

Examination of the urine was as before. The white-cell count was 42,000 with 97 per cent polymorphonuclears. The blood sugar was 1047 mg. per 100 cc., falling to 731 mg. in two hours, after administration of 30 units of protamine insulin and 66 units of ordinary insulin. The carbon dioxide combining power was 17 milliequiv. per liter. A lumbar puncture gave clear fluid under an initial pressure of 230 mm. of water.

Consciousness was never regained. The fever remained high. Therapy included 500 cc. of 2 per cent magnesium sulfate solution, and repeated doses of insulin. Death occurred on the second hospital day.

DIFFERENTIAL DIAGNOSIS

DR. THOMAS V. URMY: I think we all agree that this man had diabetes mellitus, and that it probably began much earlier than at the age of thirteen. He may have had it at two. At no point until the end was there any great difficulty in controlling the glycosuria. One would have to say that this was not more than a moderately severe case.

Probably the most striking feature in the whole history is the story that the younger sister and father developed very similar clinical pictures. It immediately raises the question whether or not we are encountering a definite syndrome or pathologic entity characterized by diabetes, renal lesions and vascular changes instead of a mere coincidence of separate diseases. Such a syndrome has been described in the past few years, although in what little reading I have done, I do not remember any account of family predisposition. This newly recognized disease has been called intercapillary glomerulosclerosis. Its clinical manifestations have been diabetes, hypertension, albuminuria and retinal vascular changes. The albuminuria and retinal changes have usually been rather marked, particularly the latter which are out of proportion to the appreciable length of time most of these people survive discovery of the condition. Edema is another common finding and often reaches a degree suggesting nephrosis. Thus, this patient's story can be explained by this condition, although we should possibly consider some other things.

Ordinarily, we should have to rule out chronic glomerulonephritis, with a nephrotic element terminally. It is rather difficult to do this clinically. The patient gave a history of what appears to have been a streptococcal infection at the time of

his fourth admission, when he was twenty-six and a half years old. At the same admission, it was found that he had slight hypertension, as well as some albumin and casts in the urine. The peculiar feature then was that he already had marked vascular changes in the retinas. It is difficult to believe that such changes could have progressed so far since the onset of the streptococcal infection. We also have a history consistent with recurrent urinary-tract infections. On one entry, it appears that the patient must have had pyelonephritis. Therefore, I wonder if this contributed to his evident renal failure.

Of course, hypertension is very much commoner in diabetes than in the general population. Was this, simply, hypertension developing in a patient with diabetes since an early age? Early x-ray studies reported here did show marked arteriosclerotic changes. One must also consider kidney failure developing secondary to hypertension, with later a nephrotic picture due to a possibly coincident amyloid disease.

I think, as I have said, that it is difficult to rule out completely the other possibilities, but there are certain things that make it more likely that the condition of intercapillary glomerulosclerosis was present. One is the relatively long survival—two years—after marked retinal changes were demonstrated. The serum protein was very low. Probably, there was more albuminuria than is seen in the ordinary case of chronic glomerulonephritis. Edema was more prominent, too.

Against the diagnosis is the age of the patient. I have not reviewed all the cases reported, but in a series that Newburger and Peters¹ reviewed in 1939, all patients were in older age groups. The youngest one did not develop even diabetes until after the age of forty. It seems quite unusual to have the diabetes begin so early in childhood and to have the whole course of the disease completed before the age of forty. The sex is also somewhat against this diagnosis, since the condition is described as much commoner in females than in males. The family history is, to my knowledge, unusual. However, I do not believe that these inconsistencies overbalance the points in favor of intercapillary glomerulosclerosis.

DR. ALLEN G. BRAILEY: A number of cases in childhood have been reported. I cannot give the reference, but I recall reading it recently.

DR. TRACY B. MALLORY: Dr. Beckman, you have seen a case at a comparatively early age.

DR. W. W. BECKMAN: Yes; it started in a person with diabetes from childhood. The patient, slightly over thirty, is still alive, with such severe retinal changes that he is almost completely blind.

RHUS TOXIN

To the Editor: Today, I saw a man with an urticarial type of skin eruption. His local physician, who referred him, had said that he had poison-ivy dermatitis and that, to save time, he might as well receive an injection of rhus toxin. The physician also stated that the toxin was a specific for poison-ivy dermatitis and that, even if he did not have this type of eruption, the injection would do him no harm.

I believe this false sense of security prevails among the medical profession at large, owing to the enthusiasm of detail men from the various drug houses. If this physician were to attend any large dermatologic clinic, practice dermatology or give injections of this antigen to a large series of patients, I am sure that he would be convinced that his statement was not true. These injections do a great deal of harm in many cases.

For example, within the past week I have seen at least ten bad results from them. One patient received an injection in the arm, with a resulting erythema and edema that was very disabling and painful. Another patient received a series of injections, and six days after the last, when the dermatitis had healed, was seized with a severe urticarial reaction that persisted for a considerable length of time. Still another patient had a widespread attack of what was formerly called "chronic eczema" but is now labeled "neurodermatitis." It came on three weeks after a series of injections with rhus antigen. This neurodermatitis is probably the beginning of a disabling dermatitis, which will prevent the patient, a student nurse, from completing her training.

I have also seen cases of exfoliative dermatitis occurring after this type of injection.

Rhus toxin cannot be given without the ever-present danger of a later allergic reaction. It should be used with caution. I have found it to be of little value in therapy, and its use as a prophylactic is still being disputed by many dermatologists.

J. G. DOWNING, M.D.

520 Commonwealth Avenue
Boston

REPORT OF MEETING

BOSTON CITY HOSPITAL

The second in the series of lectures sponsored by the Boston City Hospital House Officers' Association for the preparation of those entering the armed forces was held at the hospital on May 7, with Dr. Henry Marble discussing "Traumatic Surgery."

Two of the most trying problems of the World War I have been minimized by the routine blood typing of all men and the administration of tetanus toxoid for active immunization.

The first-aid treatment of fractures of the extremities has not changed much. Some type of Thomas splint for all fractures between the ankle and hip or of the Murray-Jones splint for those between the wrist and shoulder is still the immobilization of choice. The only things that need be emphasized are the use of adequate padding and the keeping on of the splint for the shortest possible period. In compound wounds, iodine is painted around the skin edges only, and a dry sterile dressing applied. Most, if not all, men in combat will be supplied with some sulfonamide powder, at least 1 gm. of which should be inserted in such wounds. The patient should be treated for shock, with double the usual amounts of morphine, warmth and adequate splinting, and for incipient sepsis with sulfonamide orally.

The first-aid station or field hospital is essentially a "triage station," where the patients are segregated into

shock cases, chest wounds, abdominal wounds, minor wounds and so forth. An experienced man does this important phase of the work. The order of operations is generally abdominal, chest, head and extremities. All cases of actual or incipient shock are treated in special rooms with plasma or blood, as well as the usual supportive measures.

Dr. Marble discussed particularly wounds of the extremities, which are usually not considered emergencies. Some amputations, which are performed at the field hospital, are of the guillotine type. It is definitely established that the use of the sulfonamides at the first-aid station lengthens to as long as seventy-two hours the period in which a wound may be treated as fresh and a primary débridement done. Anesthesia is a difficult problem largely because of transportation limitations. Ether is bulky and explosive, and nitrous oxide is also bulky. Spinal anesthesia is fine for the lower extremities if available, and Pentothal is satisfactory in the arm. Both, but particularly the latter, require what probably is not generally available—an experienced and competent anesthetist. This all indicates that chloroform, which is infinitely easier to transport, will be in wide use. Its dangers, furthermore, are probably overemphasized, according to Dr. Marble.

The first consideration, of course, is an evaluation of the case for shock and continuance of its treatment. Compound wounds are débrided and copiously irrigated. But, here again, what is written in the books may often not materialize because of lack of the "sharp knife and unlimited quantities of sterile fluid." The best must be done, often with inferior equipment. Again the wound is dusted with one of the sulfonamides, which is also given by mouth. The wounds are left open, despite the fact that they are now being closed by some men even in the presence of gas bacilli when the sulfonamides are used. This is not yet practical on a large scale. The number and virulence of gas bacilli vary remarkably with the locality.

The fracture itself at the field hospital is best returned to its traction splint, possibly with skin traction instead of the ankle or wrist hitch. Further transportation is in the offing, and the use of plaster-of-Paris casts has not proved practical when the state of the wound is questionable, and when constant observation during transport is not possible. When good results have been reported with this method, the wounds have been fresh, and there has been no further transportation. If adhesive skin traction has been instituted, the patient is always ready for transfer to bed traction. In Dr. Marble's opinion, closure of wounds is permissible only when they have been proved bacteriologically to be reasonably free of at least serious pathogenic organisms. Such facilities are usually found only at base hospitals farther back. Plating of fractures may be carried out in the rare event that the equipment is at hand, but even then the wound should be left open.

Whenever severed nerves are encountered, an attempt should be made at a suture of some sort. It has been demonstrated that these structures do almost as well in septic as in clean wounds, and any identifying material on the nerve ends facilitates secondary repair of the nerve. For this reason, some means of identification should always be introduced, for improperly treated nerve injuries result in the severest sequelae.

Tendons, on the other hand, have notoriously poor results in septic areas. But this should not prevent one from attempting suture, for nothing is lost and the ends may be kept somewhere near approximation for secondary repair. In any event, Dr. Marble is not yet ready to advocate primary closure of the superficial tissues in compound wounds of any kind.

(Notices on page x)

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THE PHYSICIAN'S STATUS IN CHILD-GUIDANCE WORK*

PHILIP SOLOMON, M.D.†

BOSTON

PROBABLY no field of human endeavor is in such a state of confusion as that of child guidance, which had scarcely been heard of fifty years ago. Today, everybody wants to guide the child. The discovery that "the child" was a fallow field for exploitation aroused enthusiasts from many walks of life. Teachers, social workers, district nurses, clinical psychologists, lay psychoanalysts, and religious leaders, have laid claim to the ability to solve the problems of childhood. The United States Government itself has recognized the importance of this movement and has gone to considerable pains to organize a White House conference on the child, which has taken place in Washington once in each of the last four decades. The medical profession has not stood idly by during this time. Having long ago recognized the specialized nature of the physical problems of childhood by the creation of pediatrics, physicians now see in the mental, emotional and behavioral problems of childhood the need for a special branch of psychiatry.

Child psychiatry is one of the youngest of the medical specialties. Most of the work done in this field has been descriptive, explanatory and theoretical. The present status of child psychiatry may be likened to that of general psychiatry before Kraepelin, since there is not even the beginning of agreement regarding the proper classification of the various problems involved. Diagnosis and treatment are still more of an art than a science, and much of the work done is strictly on an empirical basis. Here and there, one sees attempts to introduce scientific methods of observation and controlled experimentation, but these researches stand out conspicuously in the literature against the background of untested theory, unverified speculation and thoroughly prejudiced points of view.

Under these circumstances, one may well ask whether a physician is necessary in child-guidance work. If such work is largely spiritual, perhaps a minister would be better qualified, if educational, a teacher, and if sociologic, a social worker or recreational leader. Surely, many problems of thumb sucking and bed wetting can be dealt with adequately by the district nurse, and many truants and delinquents can be handled by the truant officer, policeman or probation officer. What are the special abilities of the physician in these matters, and does the need for such abilities arise sufficiently often to warrant the presence of a physician in a child guidance clinic?

PROCEDURE

In an attempt to answer these questions, the records of 100 consecutive cases seen at the Habit Clinic for Child Guidance, Boston, were studied.‡ The patients were all seen within a period of approximately two years. They represent a fair cross section of the cases seen in the clinic and in others dealing with children in this age group. The ages ranged from one to eleven years, with an average of six years. There were 73 boys and 27 girls. The problems presented included the usual ones of habit reactions (poor eating, sleeping and elimination, and disobedience), predelinquency (stealing, lying and truancy), personality peculiarities (shyness, boldness, cruelty and neurotic complaints), educational difficulties (poor school progress and specific defects), tics, mannerisms and speech disturbances. The approach in each case was threefold: physical, intellectual and emotional.

Since the details have been described at length elsewhere,§ it will suffice to point out that each child was examined physically by either the fam-

*From the Habit Clinic for Child Guidance, Boston, and the Department of Psychiatry, Tufts College Medical School.

†Habit Clinic for Child Guidance, junior visiting neurologist, Boston City Hospital, assistant in neurology, Harvard Medical School, instructor in psychiatry, Tufts College Medical School.

‡When two or more children in the same family were patients only the first child referred was included in this study so that the 100 cases represent a hundred different families.

§Ethom D. A. *Habit Clinics for Child Guidance*. 97 pp. Washington: Children's Bureau, United States Department of Labor, 1939.

ily physician or a physician in the outpatient department of a hospital situated conveniently near the family. In some cases, the psychiatrist did part or all of the physical examination himself, or requested that a special examination, including blood and urine tests, lumbar puncture, x-ray films and electroencephalograms, be done elsewhere. The clinic psychologist administered a battery of intelligence tests to each child. The psychiatric social worker studied the home, school and neighborhood, and brought back the pertinent sociologic data. The psychiatrist evaluated this material and, in addition, attempted to gain knowledge of the child's emotional life through interviews with the child and parents. All this represents the usual procedure in child-guidance clinics.

In this study, the cases were classified in two ways. Each case in the first classification was put in one of the following groups:

Group A. Cases in which the problem was considered to be due primarily to organic disease in the child.

Group B. Cases in which the problem was considered to be due in part to organic disease in the child.

Group C. Cases in which organic conditions were found in the child, but in which these were incidental and not related to the basic problem.

Group D. Cases in which organic factors in the child played no part but in which incidental medical advice was given to other members of the family.

Group E. Cases in which organic factors in the child and medical advice played no part.

In the second classification, each case was put into one of the following classes:

Class H. Cases in which only a knowledge of the proper methods of child management was necessary.

Class M. Cases in which the knowledge and training of a physician were required.

Class Q. Cases in which only the knowledge and training of a psychologist were necessary.

Class P. Cases in which the knowledge and training of a psychiatrist were essential.

Examples of the various groups and classes are as follows:

CASE REPORTS

GROUP A, CLASS M.

A. C. (Case 2866), a 9-year-old boy, was referred to the clinic by his mother, at the suggestion of the Community Health Association, because of bed-wetting. A routine physical examination was negative, psychologic examination revealed good normal intelligence, and psychiatric interviews revealed no emotional data of great consequence.

It was believed that the patient's enuresis was due to faulty training or insufficient motivation. The usual enuresis regime was instituted, and the patient was given a great deal of suggestion and encouragement. After 6 months of treatment, however, there was no improvement in spite of what seemed to be excellent co-operation on the part of both the patient and the mother. The child was therefore referred to a genitourinary surgeon for special investigation of the genitourinary tract. It was found that the patient's urinating was characterized by a weak stream and dribbling. A urethrogram showed a definite narrowing of the anterior portion of the urethra, apparently a congenital stricture. The patient was dilated, by bougies of increasing size, and his symptoms rapidly improved.

GROUP A, CLASS P.

F. B. (Case 2994), a 7½-year-old girl, was referred to the clinic by the Boston City Hospital. The child had been taken to the hospital by the parents because of increasingly severe behavior problems, which had finally caused her to be expelled from school. She was mischievous, defiant, unruly, extremely hyperactive, distractible and impulsive, and much of her behavior was bizarre. There was a past history of convulsions, dating from the age of 1½ years. Recently, there had been a few minor seizures of a petimal nature. A 3-year-old brother had convulsions regularly. Because of the severe degree of the patient's behavior problem, an attempt was first made to have her institutionalized. This was not immediately successful.

An electroencephalogram showed abnormal waves, some of which were of the wave-and-spike pattern characteristic of petit mal. Apparently, the child was having these abnormalities disturbing the function of the cortex almost constantly, although not to a sufficiently severe degree to produce clinical seizures. She was started on dilantin sodium, and the dose was increased until she was taking 0.2 gm. a day. A remarkable change occurred in her behavior almost immediately. The child became "a different girl." Her misbehavior stopped, and she apparently quieted down and became co-operative and obedient. She seemed to be in every way a perfectly normal child. Under the medication, this improvement continued, except for two intervals when the medicine was stopped—once because the parents ran out of it, and once when the child had a cold. On both occasions, the previous difficult behavior occurred. Because of the improvement, the child was allowed to go back to school on trial, and she made an excellent adjustment there. A check-up of the electroencephalogram later revealed normal brain waves.

GROUP B, CLASS M.

N. W. (Case 2689), a 5-year-old girl, was referred to the clinic by her mother because of night terrors and because she was generally tense and high strung. It was found that the mother had been unusually severe in her disciplining of the child. The child had been given glasses for a strabismus. However, one of the lenses had become rotated following a fall. Consequently, the strabismus had become worse, and there was a noticeable increase in the child's "nervousness." The glasses were immediately changed, and the mother was urged to modify her management. The child soon responded with improved general behavior and the disappearance of the night terrors.

GROUP B, CLASS P.

T. D. (Case 2837), an 8-year-old boy, was referred to the clinic by his mother because of unwillingness to go to school, crying spells, irritability and "general maladjustment." The parents were well educated, tense and over-

serious in their attitude toward their only child. Recently, the child had begun to bite his fingernails, twitch his face, screw his mouth about, pull at his eyes, hunch his shoulders, and "generally wiggle." It was found that he was in good physical health, but was still taking thyroid tablets, which had been prescribed for him when he was 4 years old because of "lack of pep." On psychologic examination the patient had an intelligence quotient of 143. The thyroid medication was stopped, and much work was done with the parents and the child in attempts to alter their attitudes. As time went on, the patient's symptoms gradually dwindled, and the parents gained confidence in the clinic. They soon began to lean on us for advice in all the minute details of the child's life. Eventually there was a great improvement in the entire family situation.

GROUP C, CLASS H

H H (Case 2776), a 2½ year-old boy, was referred to the clinic because of feeding difficulties and bed wetting. The patient was an only child, and the mother was erratic and inefficient in her daily schedule with the child. She was given routine advice regarding the child's eating and elimination, and many suggestions were made to her about the improvement of her schedule. The patient was entered in an all day nursery school, and at the mother's request the psychiatrist examined him physically and filled in the blank required by the nursery school.

GROUP C, CLASS P

R B (Case 2781), an 8½ year old boy, was referred to the clinic by his teacher because of poor work in the class room. The mother added that the boy bit his nails and sucked his thumb.

The patient was the only child of a middle aged couple. The mother had a great many interests and was not concerned about her maternal duties. It was difficult to get her to take the child's problem seriously or to follow clinic recommendations. The patient was found to be physically well and of superior intelligence. It was believed that his work habits were poor, and that he was a fundamentally unhappy boy. In the course of a year's contact with the case, the mother's attitudes were modified but little. The father could not be seen, but after repeated interviews, the child was given some insight into his mother's make up. Through the Cub Scouts, summer camp, tutoring in reading and direct psychotherapy, the boy began to make a better adjustment to his life situation.

GROUP D, CLASS M

C C (Case 2758), a 6½ year old boy, was referred to the clinic because of soiling. The child was the second of six children living in an extremely dirty, poverty stricken and badly managed home. The mother was unintelligent, and the father was being treated for pulmonary tuberculosis. It was found that the patient was sleeping on a small cot with the father. The psychologist found the patient to have superior intelligence. It was believed that the soiling was a reflection of the unsatisfactory home conditions. The child was placed in a preventorium for children suspected of tuberculosis. While he was there, his problem rapidly disappeared. Arrangements were made for the father to resume proper treatment for his own tuberculosis, since he had allowed his pneumothorax to lapse.

GROUP D, CLASS P

M W (Case 1561), a 10 year old boy, had been a patient at the clinic at the age of 3, when he was an eating problem and responded readily to routine advice. Seven years later, his mother brought him back because she believed

that he had an "inferiority complex." She also complained that he was disobedient and unruly. It was found that most of the child's difficulties were a reflection of the mother's unstable and neurotic temperament. Work with this case covered several years, during which direct treatment was given to the mother, particularly during a period of depression that followed a pelvic operation. Since the patient entered adolescence at this time, a great deal of work had to be done to interpret the changes in the child to the mother and to the patient himself. The father was seen several times, and his assistance was solicited in helping the mother in her problems and in taking over part of the responsibility for the patient's difficulties. In the course of time, a much better relation was set up in the home, and the patient's adjustment to the outside world, and to himself, was greatly benefited.

GROUP E, CLASS H

T W (Case 2671), a 2½ year old boy, was referred to the clinic for sucking his lower lip persistently. It was found that the mother was an extremely emotional, irritable and unstable person who kept the home in a constant state of tension by scolding, nagging and spanking. The mother failed to co-operate with the clinic. She did not keep appointments, she would not accept a nursery school placement for the child, and it was not possible to get the father to come to the clinic. Efforts to reeducate the mother in her methods of managing the child were there fore unsuccessful, and it was not possible to work with the mother in her own problem.

GROUP E, CLASS Q

R G (Case 2648), a 5 year-old girl, was referred to the clinic by the mother because of the problem of school placement. The child had attended kindergarten for 27 weeks during the previous year, having been absent several times because of illness. The child was under age for entering the first grade, and the school made a ruling that only children who had attended kindergarten for 30 weeks should enter the first grade. The mother believed that the child was bright, but did not want her to go ahead with first grade work unless she were really ready for it. On the Stanford-Binet test, when the patient was 5 years old, she scored a mental age of 7 years, 2 months, giving her an IQ of 143. The child was sturdy, well poised, friendly, responsive and well mannered. She worked efficiently and rapidly at the test procedures. On the Goodenough drawing test, Merrill-Palmer scale and mare and foal test, her results were comparable to those on the Stanford-Binet. The psychologist believed that the child showed exceptionally well developed mentality, with superior personality traits and work habits. It was recommended that the child be allowed to enter the first grade. The clinic recommendations were referred to the school committee by the school principal, and the child was accepted in the first grade. She subsequently made an excellent adjustment, and her teacher stated that she was very bright. At the end of the year, the patient was promoted in spite of the fact that she had missed a good deal of attendance because of scarlet fever, measles and whooping cough.

GROUP E, CLASS P

R H (Case 3105), a 3-year old boy, was referred to the clinic by the mother at the advice of a psychoanalyst who had been treating the mother for 5 years. The complaints were unmanageable behavior, temper tantrums, nervousness and biting of the fingernails. There was a strong family history of mental disease. The mother had had several psychotic episodes, a maternal great aunt had also

been psychotic, the maternal grandmother had been psychotic in her youth, a maternal uncle was considered mentally abnormal, and a paternal uncle had had several psychotic episodes.

The child was found to be in good physical health and to have superior intelligence on psychologic tests. Observations during clinic attendance indicated that the child was wilful and largely untrained. However, he responded well to friendly management. Treatment of this child involved for the most part education of the mother in proper methods of child training. This was a rather difficult matter, since the mother's mental status was still far from normal. During the work with the case, the mother remarked that she was still having visual hallucinations, although these did not seem to influence her behavior. Another source of difficulty came from marital discord between the parents. The father was interviewed, and through the intervention of the clinic, the parents arranged matters between themselves in such a way that the child was spared any of the consequences of their quarrels. As time went on, the patient improved, although he continued to have temper tantrums occasionally. Finally, temper tantrums also disappeared, and the mother believed that the patient was behaving quite normally. Her methods with the boy had been entirely reorganized, but her own mental condition was still far from normal. She was urged to continue to see a psychiatrist for her own mental health.

RESULTS

Table 1 shows the distribution of cases according to class, group, and results. Since the

TABLE 1. Analysis of Cases according to Class, Group and Results.

CLASS	RESULTS	GROUP A	GROUP B	GROUP C	GROUP D	GROUP E	TOTAL
H	Improved	0	0	5	0	10	15
	Unimproved	0	0	0	1	3	4
M	Improved	5	3	0	1	0	9
	Unimproved	0	0	0	0	0	0
Q	Improved	0	0	1	0	2	3
	Unimproved	0	0	0	0	1	1
P	Improved	15	6	14	3	25	63
	Unimproved	0	0	0	1	4	5
All	Improved	20	9	20	4	37	90
	Unimproved	0	0	0	2	8	10
Totals		20	9	20	6	45	100

number of cases studied is 100, the various totals are percentages.

The 20 cases in Group A are of special interest. Ten of these children presented "organic behavior" or "postencephalitic behavior" problems. In only 2 was there a history of encephalitis. In 1, a birth injury was held responsible for the brain damage, and in 7 the central-nervous-system defect was considered to be innate, perhaps hereditarily acquired. In 9 of this group, the diagnosis was substantiated by electroencephalograms taken at the Boston City Hospital through the kindness of Dr. Fred-eric A. Gibbs.

The remaining 10 children in Group A are also of interest. Five were boys, with persistent enu- resis, in whom routine treatment was of no avail.

These children were studied by Dr. M. Leopold Brodny at the Beth Israel Hospital, a new x-ray technic for visualization of the genitourinary tract being used. Urethrography in each of these cases revealed an abnormality that was amenable to surgical approach. Two had a pin-point urethral meatus, and 3 had a urethral stricture farther back. All 5 had marked dilatation of the urethra behind the stricture. The other 5 children in Group A had the following conditions: a birth injury; defective vision, and deafness in one ear; word deafness; chorea; and an old depressed skull frac- ture.

It is noteworthy that all the children in Group A were improved. Treatment in the organic be- havior problems was in part pharmacologic, dilantin sodium or amphetamine (Benzedrine) sul- fate, or both, being administered in 7 cases. Surgery was resorted to in the 5 enuretic children. Corre- ctive glasses were obtained for the child with poor vision. Neurosurgery in the child with the old depressed skull fracture was contemplated but was postponed following both electroencephalography and pneumoencephalography. This patient, whose presenting problem was somnambulance, did well on phenobarbital and a program providing in- creased rest. The child with word deafness was given special educational attention. All the chil- dren were also treated by modifications in their environment, to allow them to adjust themselves better in spite of their handicaps.

Of the 20 cases in Group A, the 5 children with genitourinary abnormalities were placed in Class M, since they certainly needed the attention of a physician. The other 15 were placed in Class P, since each case required psychiatric treatment. It should be said that the term "psychiatric" includes "neurologic." (I emphatically agree with the Examining Board for Certification in Neu- rology and Psychiatry that every psychiatrist should be a well-trained neurologist. The material pre- sented in this paper demonstrates how necessary this is in the field of child psychiatry.)

In the 9 cases in Group B, although the chief cause of the child's difficulties was regarded as an emotional one arising from environmental rela- tions, organic disease played a significant contribu- tory role. Three of these children were put in Class M, since it was believed that a competent pediatrician could have taken care of their prob- lems adequately. One had chronically infected ton- sils, for which an operation was arranged. One was developing strabismus because a lens in her glasses had become rotated following a fall. One had "worms," for which the mother was using an ineffectual proprietary medicine obtained on the advice of a druggist; proper treatment was

instituted. The other 6 children were placed in Class P, since the emotional problems involved were severe enough to require prolonged psychiatric therapy. The organic conditions were as follows: harelip (a reoperation was arranged), instability produced by prolonged thyroid therapy recommended four years previously by the family physician (the medication was omitted following consultation with the physician), a series of minor illnesses in a child who was being badly pampered by the parents, severe eczema, poor motor coordination on a congenital basis, and flat feet (an orthopedist was substituted for a podiatrist). All the children in Group B improved.

There were 20 children in Group C, in which medical advice was given for organic conditions not related to the child's problem. Five of these were placed in Class H, since the problems involved simple readjustment of the child's routine. The medical situations concerned questions of proper daily schedules, for the most part. Four of these 5 children were three years of age or younger. Fourteen were in Class P, since they needed psychiatric care, and 1 was in Class Q. Advice in these cases was given on the following medical matters: keloid, congenital nystagmus, abscess on the buttock, positive blood Wassermann reaction (3 patients), pertussis vaccination, worms, posture abdominal pain (2 patients), constipation, chicken pox, positive tuberculin reaction and polydipsia. There was improvement in all cases.

Incidental medical advice was given to relatives of 6 children in Group D. This was in the form of a discussion with the parents of their own medical problems. In each case, the parent was referred back to his own physician, and reasons were offered in favor of the treatment contemplated or already in progress. The effect was therefore one of added authority and reassurance. The conditions were as follows: pulmonary tuberculosis in a father who had omitted his pneumothorax refills, anemia, alcoholism, multiple sclerosis, fibroids of the uterus, and severe neurosis. Two children in this group were unimproved. One was the child whose mother had the neurosis, and the other the child whose mother had the anemia. In neither case did the parents cooperate with the clinic.

The remaining 45 children were in Group E, in which no organic conditions or medical advice played a part. None of these children, therefore, were in Class M. The largest number of unimproved cases (8) fell in this group.

Of the total 100 children, 19 were in Class H. The problems in these children could have been adequately handled by a district nurse, a nursery school teacher or anyone well versed in the proper methods of child management. Neither a phy-

sician, a psychologist nor a psychiatrist proved necessary, except to rule out abnormalities in their special fields.

There were 9 cases in Class M, in which the knowledge and training of a physician were necessary in the treatment. In 5 of these (the enuretic children in Group A), the referral of the child by a nonmedical "child guidance expert" to an average physician for a check up would not have elicited the organic lesion found. Many pediatricians, however, would be in a position to do justice not only to all the children in this class but also to all those in Class H.

Class Q contained only 4 children, 2 of whom were doing poorly in school in spite of normal intelligence. It was found that both were "non readers," and remedial reading instruction was arranged for them. One five year-old child was too young to be admitted to the first grade in her community, and yet the mother believed she was extremely bright and could easily do the work. The psychologist found that her mental age was over seven—an intelligence quotient of 143. The school committee accepted a recommendation that the child be admitted to the first grade, and she subsequently did very well. The fourth child in this group proved to be feeble minded, and institutional care, although recommended, was not accepted by the parents. In all 4 cases, the services of the psychologist were both necessary and sufficient. Of course, in many more of the total group of patients, the psychologist contributed information of considerable value, but in all these cases, other services were necessary.

The large number of children in Class P (68) was surprising. Of course, the cases were necessarily judged in a rather arbitrary way. It may well be that someone else going over these records might not believe that all these children needed the ministrations of a psychiatrist. Nurses, psychologists and nonpsychiatric medical men could probably have done a satisfactory piece of work with many of these children. However, so far as they were able to show insight into the emotional causes for the child's problems, both in the child and in the parents, and were able to institute proper therapeutic measures for their relief, such persons would be acting the role of a psychiatrist. Certainly, many of these problems can be seen through by well directed common sense. However, treatment by a psychiatrist offered the best chance for solution of the fundamental problems in these 68 cases, and in some, treatment by anyone other than a psychiatrist would probably have been grossly inadequate.

It should be added that the average psychiatrist sees very few children and might therefore be

quite unprepared to administer the kind of psychiatric care that these children required. In fact, without special training in child psychiatry, many psychiatrists would be in a worse position for helping this group of children along emotional lines than some psychologists and pediatricians. In addition, the average psychiatrist has lost touch with the organic pediatric problems in children, so that although he is a physician, he would not be able to do justice to the children in Class M, discussed above. The child psychiatrist, however, can contend not only with the problems in Class P but also with those of Class M and Class H.

It will be noted that 10 cases were unimproved. In none of these was there occasion to give medical advice to the child. In 2, as noted above, the mothers were given incidental medical advice; in 8, failure may be attributed to lack of co-operation on the part of the parents or to inability to secure this co-operation. In 2 of the unimproved cases, failure was due to the inherent nature of the child's problem.

DISCUSSION

The question regarding the role of a physician in a child-guidance clinic may be answered by a reference to the statistical data. In 20 per cent of the cases, the child's problem was due primarily to organic disease. In an additional 9 per cent, the problem was due in part to organic disease. In 20 per cent, incidental medical advice was given to the child, and in 6 per cent to other members of the family. A total of 55 per cent of the cases (Groups A, B, C and D), therefore, required medical care.

The question naturally arises whether medical care could be furnished in child-guidance clinics in which there is no physician in attendance by the practice of referring each child to an outside physician for a routine physical check-up. In a number of clinics directed by "clinical psychologists" or other nonmedical persons, this practice is followed. The results, however, depend largely on the interest and thoroughness of the outside physicians. Our own experience with "routine physical check-ups" indicates that examinations are sometimes done rapidly, incompletely and without any particular interest in the possible special examinations or laboratory data that might throw light on the etiology of the child's behavior problem. In clinics where one or two outside physicians are relied on for this type of work, such objections may not apply, and the arrangement may work out very satisfactorily. In clinics where the director is a physician, however, children have the advantage of being seen periodically by one who will keep the possibility of organic disease constantly in mind.

When one considers that, in 29 per cent of these

cases, organic disease played an important part in the etiology of the behavior problem and that medical advice was given in an additional 26 per cent, it seems fair to say that a physician should be closely associated with every child-guidance organization and, preferably, should be an integral part of it.

Should the physician be a general practitioner, pediatrician or psychiatrist? Nineteen per cent of the patients (those in Class H) could have been treated adequately by anyone familiar with proper methods of child management; district nurses, social workers, schoolteachers and even helpful neighbors frequently do a good job with this type of case. Nine per cent (the children in Class M) needed nonpsychiatric medical care. In 5 per cent, it was believed that a pediatrician would be likelier to do justice to the case than a general practitioner. In part of the 19 per cent of Class H, the same opinion applies. Four per cent of the patients (those in class Q) specifically required psychologic services. The psychologist, of course, contributed information of value in many other cases, and if negative or corroborative data are included, it is fair to say that the psychologist was helpful in every case. It should be added that some psychologists are thoroughly capable of properly handling the cases in Class H and the majority of cases in Class P. Sixty-eight per cent of the patients (Class P) needed specialized psychiatric care. The interpretation of this type of care has been discussed above. A psychiatrist trained in

TABLE 2. *Various Workers in Charge of Child Guidance Appraised according to Probable Ability to Manage Different Types of Cases.*

DIRECTOR	CLASS H %	CLASS M %	CLASS P %	CLASS Q %	TOTAL %
Lay worker (nurse, teacher and so forth)	19	0	10	0	29
Lay worker in addition to medical referral. . . .	19	4	10	0	33
General practitioner. . . .	10	4	20	0	34
Pediatrician	19	9	25	0	53
Psychiatrist (not trained in child guidance)	15	4	50	0	69
Psychologist	19	0	48	4	71
Psychologist in addition to medical referral.	19	4	48	4	75
Child-guidance psychiatrist. . . .	19	9	68	0	96
Child-guidance psychiatrist in addition to psychologist	19	9	68	4	100

child-guidance work is also capable of doing justice to the cases in Class H and Class M.

A summary of the statistical data as they might be applied to an appraisal of various workers in their ability to handle the problems of a child-guidance clinic is presented in Table 2. Many of these figures are, of course, rough estimates. It is assumed that each worker is highly skilled

in his field. It may be seen that skilled lay workers could manage all the cases in Class H and 10 of those in Class P, making a total of 29 per cent that could be properly managed. This is probably accurate to within 5 per cent. When the lay worker uses a routine medical check up, the total of cases properly managed is raised to 33 per cent, since 4 of the cases in Class M are added. Similarly, the general practitioner, pediatrician, psychiatrist, psychologist and child psychiatrist are appraised. According to this estimate, child guidance clinics run by psychologists with assisting medical men but without psychiatrists will adequately provide for about three fourths of the patients seen at the clinic. To do justice to all the problems that may arise, both a psychologist and a child psychiatrist should be part of the clinic.

No attempt has been made to appraise the value of the psychiatric social worker in the child guidance clinic. It may be said quite categorically that such a clinic could not function without a social worker. But it is difficult to estimate how essential the work done by the psychiatric social worker in the investigation of the home, school and neighborhood was to the proper management of these 100 cases. In private work, the psychiatrist or clinical psychologist is frequently able to gather the social data himself, although this is time con-

suming and often less thorough than the study made by a psychiatric social worker.

SUMMARY

In an attempt to evaluate the proper status of the physician in child guidance work, a study was made of 100 consecutive cases seen at a child guidance clinic. The cases were classified according to the part played by organic disease in the etiology of the child's problem, and according to the type of knowledge (lay, medical, psychological or psychiatric) needed in the proper management of the case.

In 29 per cent of the cases, organic disease played a major part in the etiology of the child's problem, and medical advice was given in an additional 26 per cent. Nineteen per cent of the cases could have been treated adequately by anyone familiar with proper methods of child management, 9 per cent needed nonpsychiatric medical care, 4 per cent needed the attention of a psychologist, and 68 per cent needed treatment by a psychiatrist.

A physician should be closely associated with every child guidance clinic and, preferably, should be an integral part of such a clinic. It is desirable that the physician should be a psychiatrist, specifically trained in the management of the problems of childhood.

OBSERVATIONS CONCERNING PULMONARY FIBROSIS IN RAYNAUD'S DISEASE*

Report of Two Additional Cases

HARRY LINENTHAL, MD†

BOSTON

THREE cases of pulmonary fibrosis in patients who were suffering with Raynaud's disease were reported recently.¹ The histories were uniform. They all started with typical manifestations of Raynaud's phenomena, and after several years, nutritional changes of the skin began to manifest themselves with the development of scleroderma. Some time later, the patients began to complain of dyspnea on exertion. Roentgenologic examinations showed some evidence of fibrosis at the bases of the lungs. All 3 patients died within three or four years after the onset of the dyspnea. One patient had an intercurrent infection, which was the immediate cause of death.

Because these patients were suffering from vascular disease and because of the absence of any

recognizable factors that could explain the etiology of the pulmonary fibrosis, it was believed that there was a direct relation between the pulmonary condition and the coexistent Raynaud's disease. Therefore, Raynaud's disease can be considered to affect not only the small arteries of the extremities but also the small arteries of the lungs and possibly of other organs of the body. Since the above report, 2 additional cases have been observed. In one of these, now under observation, studies of the lung and pulmonary dynamics have been carried out. In the other, post mortem examination showed extensive pulmonary fibrosis secondary to vascular changes in the lungs.

CASE REPORTS

CASE 1. Mrs. F. J. W., a 30-year-old woman, was first seen in 1932. The past history was not significant except for frequent attacks of tonsillitis and joint pains, for which several infected teeth had been extracted. The presenting

*Presented in abstract at a section meeting of the American College of Physicians on April 22, 1941.

†Professor of clinical medicine, Tufts College Medical School; physician in chief, Beth Israel Hospital.

symptom was related to circulatory disturbances of the hands of 6 months' duration. On exposure to cold or when the patient was emotionally disturbed, the fingers of both hands assumed a deathlike pallor, became cyanosed and later developed a hyperemia, with marked paresthesia of the finger tips. She also noticed from time to time a transient blotchy hyperemia of the chest.

About a year later, the patient developed all over her body a diffuse recurrent urticaria, which had no apparent relation to her environment or food.

The patient was not seen again until November, 1940, when she stated that she had been treated for a number of months with elimination diets, without any improvement of the urticaria. Later, a tonsillectomy was performed, without improvement of either the urticaria or the Raynaud's disease. In 1935, the patient had begun to experience shortness of breath on exertion. In 1939, she had had an acute pulmonary infection, which had left her with a troublesome cough and with greatly increased dyspnea.

The Raynaud's disease had grown progressively worse. The hands and fingers showed a permanent purplish cyanosis, which became more marked on exposure to cold or excitement. The patient had well-developed scleroderma of the hands and face. She was unable to open her mouth freely. The skin on the face felt tightened, and the nose had become narrowed and sharper in outline. The tips of the index and middle fingers of the right hand showed small superficial ulcerations. She had lost 15 pounds in the last few years. Her catamenia had been scanty and irregular for a few years.

The heart was not enlarged, and the rhythm was regular, with a rate of 90. Electrocardiographic tracings did not show any significant changes. The blood pressure was 130/70. The lungs showed diminished resonance, with increased fremitus in both bases and with rales after coughing. The red-cell count was 5,900,000, with a hemoglobin of 90 per cent, and the white-cell count was 13,400; the differential count was not significant.

A roentgenogram of the chest (Fig. 1) in April, 1941, showed slight clouding at the upper peripheral portions of the chest in the first interspaces anteriorly on both sides. There was slight diminished radiance at the left base, with flattening and limitation of the excursions of the left side of the diaphragm. In other words, the roentgenogram of the lungs did not show sufficient changes to account for the extreme dyspnea and cyanosis.

In July and again in September, Dr. Mark D. Altschule carried out studies on the patient's pulmonary dynamics, which have been described briefly elsewhere.² The following observations are particularly pertinent: total lung volume, 2495 cc.; vital capacity, 795 cc.; complemental air, 595 cc.; reserve air, 200 cc.; midcapacity, 1900 cc.; and residual air, 1700 cc.

The total lung volume was about half normal. The complemental air was about 25 per cent normal, indicating very marked impairment of distensibility owing to abnormal rigidity of the lungs. The reserve air was about a quarter normal and likewise indicated considerable loss of elasticity of the lungs (again because of fibrosis). The loss of elasticity caused the intrapleural pressure to be less negative than normal, and the respiration was further embarrassed.

Failure of the lungs to expand and to relax properly keeps the tidal air low (in this case, 315 to 373 cc.) and makes washing out of the residual air (the air that cannot be expelled from the lungs) difficult. To prevent or minimize arterial anoxemia and retention of carbon dioxide, increased respiratory activity is necessary. The

patient exhibited this increase (respiratory rate, 23 to 26 per minute, and respiratory volume, 8200 to 9300 cc. per minute—almost twice normal). The arterial blood oxygen saturation was normal, which indicates that the patient did not, on rest, develop anoxemia because she

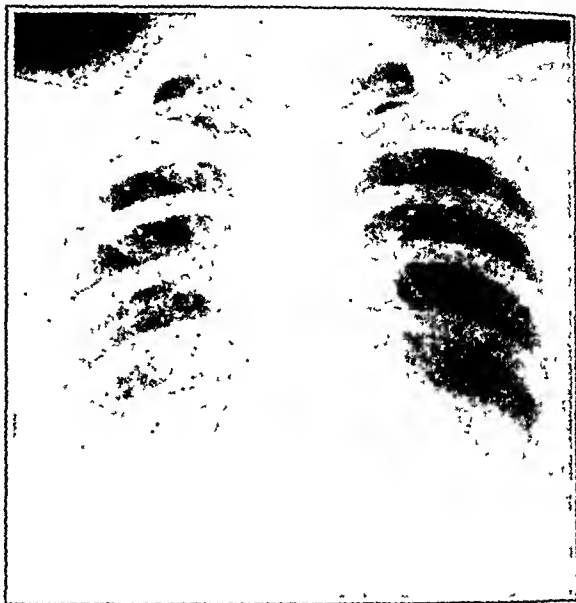


FIGURE 1. Case 1.

This radiogram of the chest shows only slight changes in the bases of the lungs, in spite of severe respiratory difficulty.

compensated for the impaired pulmonary function by increased respiratory activity.

The patient thus presents a clinical picture similar in every respect to the cases previously reported. She started with typical Raynaud's phenomena; 4 years later, she began to show progressive nutritional changes of the skin of the hands and face; and about 2 years later, respiratory symptoms, marked by severe exertional cough, developed. Study of the pulmonary dynamics and, to a lesser extent, of roentgenograms shows evidence of pulmonary fibrosis.

CASE 2.* M. R., a 45-year-old woman, was first admitted to the Beth Israel Hospital in January, 1940. She gave a history of Raynaud's phenomena of 10 years' duration. A left cervical sympathectomy was performed in 1935, and a right cervical sympathectomy in 1936, following which the hands improved a great deal. Following pregnancy 10 and 12 years previously, the patient had had two attacks of arthritis involving the hands, knees and ankle joints. Tonsillectomy and teeth extractions were performed to eliminate foci of infection. Several months before entry, the patient began to experience dyspnea on exertion that progressed and was associated with severe coughing spells. Five days before entry, she complained of substernal oppression and shortness of breath even while at rest. She had been completely digitalized before admission to the hospital.

On examination, she was found to be slightly cyanotic, and markedly dyspneic. The skin was smooth, warm, dry and slightly blotchy over the face and hands, with nutritional changes. The heart was enlarged to percussion, with a diffuse apical impulse and a rate of 100. There were frequent extrasystoles. A soft systolic murmur was

*I am indebted to Dr. Julius Abramson for permission to report this case.

heard all over the precordium. The pulmonic second sound was louder than the aortic. On one occasion, a diastolic murmur was heard at the apex. The peripheral vessels were normal. The blood pressure was 110/80. The lungs showed dullness at both bases, with medium



FIGURE 2. Case 2.

The congestion shown at the bases of the lungs was assumed to be secondary to the marked degree of cardiac enlargement.

crepitation rales. The liver edge could be felt 3 fingerbreadths below the costal margin. There was moderate pitting edema of the ankles. The hands showed arthritic deformities, and there was limitation of motion of the elbows, shoulders, knees and back.

Roentgenographic examination showed a large heart and exaggerated markings at the bases of both lungs (Fig. 2). The patient did very poorly during her stay in the hospital. She was discharged with the diagnosis of rheumatic heart disease, mitral stenosis and regurgitation, right-sided and left-sided cardiac failure and Raynaud's disease.

After discharge from the hospital, the patient was confined to bed at home. She was maintained on digitalis, in spite of which she developed generalized edema and fluid in the chest and abdomen, for which she had to be tapped.

In September, because of severe back pain, she was readmitted to the hospital for further study.

Her condition became progressively worse. The back pain became very severe, and on the 15th hospital day, the patient became irrational and had an elevation of temperature; she expired on the 17th hospital day.

Autopsy. The heart was slightly enlarged, weighing 400 gm. The right auricle and appendage were markedly dilated and hypertrophied. There were no valvular anomalies. Injection and dissection of the coronary vascular tree showed a normal number of atherosclerotic plaques. Microscopic examination showed an increase of the fibrous tissue in the endocardium and in the annulus fibrosus of the mitral valve.

The right lung weighed 340 gm., and the left lung 250 gm. Crepitation was diminished throughout. The lower lobes, particularly the left, were compressed by fluid in the pleural and pericardial cavities. The pulmonary veins

and arteries were moderately dilated. Microscopic examination showed fibrous thickening of the pleura and pulmonary tissue, with engorgement and dilatation of the vessels and infiltration with lymphocytes, monocytes and pigment-laden phagocytes. In many areas, these inflammatory cells were gathered into focal collections. The muscular walls of the bronchi and bronchioles were intact but, in many cases, showed fibrosis. The alveolar spaces were relatively normal in appearance but somewhat smaller than usual. The alveolar walls were definitely thickened and prominent, with an increase in fibrous tissue up to ten to fifteen times normal (Fig. 3). The alveolar spaces showed no evidence of inflammatory reaction. This thickening of the alveolar walls had resulted in partial obliteration of the alveolar spaces, so that many areas appeared to be atelectatic. In some places, thick buds of cells, with indefinite outlines and fibrous stroma, projected from the alveoli into the spaces. Scattered through this dense fibrous reaction were a large number of dense focal collections of these cells. There was no evidence



FIGURE 3. Case 2.

This photograph of a section of the lung shows great thickening of the alveolar walls, owing to fibrotic changes.

of an acute inflammatory process, neoplasm, abscess or infarct. The capillaries were dilated and congested, and in many areas were definitely thicker than normal, suggesting a primary vascular basis for the fibrous thickening of the alveolar walls. The most prominent features, in the lungs, therefore, were the diffuse pulmonary fibrosis, the suggestive arteriolar thickening, with heaped-up nuclei in some areas, and a slight degree of emphysema, with almost normal appearing alveolar walls.

The liver was somewhat enlarged, weighing 1500 gm., and firmer in consistence than normal. There appeared to be a slight increase of fibrous tissue.

The muscles and subcutaneous tissues showed some focal collections of inflammatory cells suggesting chronic myositis.

The significant pathological diagnoses were: enlarged heart; congestive heart failure; and diffuse pulmonary fibrosis.

SUMMARY

Two additional cases of pulmonary fibrosis associated with Raynaud's disease are reported. One case, under observation, showed pulmonary fibrosis by roentgenograms and studies of the pulmonary dynamics. The other, at post-mortem examination, showed extensive pulmonary fibrosis, with changes in the small vessels of the lungs that

were consistent with the vascular changes found in the small digital arteries in advanced cases of Raynaud's disease.

45 Bay State Road

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TUBERCULOSIS OF THE FOOT AND ANKLE IN ADULTS AND CHILDREN*

JOSEPH D. WASSERSUG, M.D.†

MIDDLEBORO, MASSACHUSETTS

IN any analytical discussion of tuberculosis of the ankle or foot, a sharp distinction must be made between disease involving the ankle (tibioastragaloid) joint and tuberculosis of the tarsal and metatarsal bones. Disease of the soft tissues and tendons must be differentiated from disease in bones and joints. Furthermore, since treatment and prognosis differ in adults and children, cases in children should be analyzed separately from those in adults, and since tuberculosis may resemble other diseases clinically and roentgenologically, cases that are pathologically proved must not be confused with unconfirmed cases. Finally, if treatment is to be evaluated, cases must be adequately followed.

A review of the literature reveals that oftener than not "ankle" is used as a generic term that includes "foot." Only recently has the need for pathological investigation and proof of tuberculous etiology been stressed.¹⁻³ Cases of disease in adults and children have been mixed together. Differentiation of cases in adults and children has been made by Delahaye,⁴ Miltner and Fang³ and Mitchell.⁵ Adults alone are considered by Dubau and Bolot,² Gaenslen and Schneider⁶ and Rogers,⁷ and children alone are discussed by Sever,⁸ Papin,⁹ Pouzet¹⁰ and Fraser.¹¹ No distinctions, however, are made by Schiller and Altschul,¹² Rollier,¹³ Petrov,¹⁴ Piquet¹⁵ and LoGrasso.¹⁶

This paper represents a study of 46 cases of ankle (tibioastragaloid) tuberculosis and 42 cases of tuberculosis of the tarsus and the metatarsal bones. Cases involving only soft tissues, tendons or the phalanges have been excluded. The patients were admitted to the Lakeville State Sanatorium between the years 1926 and 1940. Since 1134 patients with bone and joint tuberculosis were admitted in this period, this represents an

incidence of approximately 4 per cent for each form.

TUBERCULOSIS OF ANKLE

Of the 46 cases studied, 24 were in males, and 22 in females. Twenty-four cases were in the right ankle, 21 in the left, and 1 in both. The age at onset of symptoms varied from one to sixty-five years, with an average of twenty-two years. On admission, 20 patients were between the ages of one and fifteen, 22 between sixteen and forty-five and 4 between forty-six and sixty-five, the average age being twenty-five years. In 15 cases, a history of trauma was obtained. The family history was positive for tuberculosis in 15 cases. In 39 cases (85 per cent), other demonstrable tuberculous foci were present.

Through the aid of the Social Service Department, 36 cases were followed from two months to fourteen years, an average of six years, after discharge from the sanatorium. Of the 10 patients not followed, 8 died while in the sanatorium and only 2 could not be traced. Excluding these 2 cases, 18 cases were proved pathologically, and in 16 the diagnosis was made only on clinical and roentgenologic evidence. Among the 16 cases, there were 7 deaths—all due to pulmonary, meningeal or urogenital tuberculosis.

Proved cases in adults. In this discussion, an adult is arbitrarily defined as a person sixteen years or older. Of the 28 proved and followed cases, 16 patients were in this group. Fifteen of these had additional tuberculous lesions: other bone and joint lesions were present on admission in 11 cases, and 10 patients had evidence of pulmonary tuberculosis. Multiple lesions were present in 6 cases. Seven of the 16 adults with proved ankle tuberculosis died, 3 while in the sanatorium and 4 within five years after discharge. In only 2 cases, pulmonary tuberculosis or tuberculo-

*From the Massachusetts Department of Public Health.

†Formerly, assistant physician, Lakeville State Sanatorium, Middleboro, Massachusetts.

meningitis was the cause of death. Conservative treatment—that is, sanatorium regime, plaster immobilization, aspiration or incision and drainage of abscesses as indicated—was given to 6 patients, some of whom were seriously ill on admission. Four of these patients died, but good results were obtained in the remaining 2 cases. In 3 cases, an arthrodesis was performed, with poor results in every case. One case required amputation four months after arthrodesis. Amputation was performed two to ten months after admission in 5 cases, with good results in 5 and death in 3.

Unproved cases in adults. Of the 8 cases lacking pathological confirmation, 6 died of tuberculosis, 2 while in the sanatorium and the others within five years after discharge. Five cases were treated conservatively, and in only 1, followed for eleven months, were the results satisfactory. One arthrodesis, 1 amputation and 1 osteotomy were done, and all 3 patients operated on died.

Proved cases in children. Any person fifteen years or younger is defined as a child for the sake of discussion. Twelve cases of proved and followed ankle tuberculosis fell in this group. Two of these patients were hospitalized primarily for other tuberculous lesions, of which they subsequently died. The third death in this group of cases was due to tuberculous meningitis. Of the remaining 9 living patients, 4 were given conservative treatment, with good end results, a satisfactory erosion or curettage was done in 3 cases, and in 2 cases, erosion or curettage required subsequent amputation. The last 2 patients have artificial limbs and get along well.

Unproved cases in children. There were 5 cases in this group, with only 1 death, due to tuberculous meningitis. Five patients were treated conservatively, and good results were obtained in every case. Two cases, treated by erosion, were followed for more than two years, and good results were obtained.

TUBERCULOSIS OF FOOT

Of the 42 cases studied, 23 were in males and 19 in females. Twenty-eight cases were in the right foot, 13 in the left, and 1 in both. The disease may strike any bone or joint in the foot, and in 5 cases only the metatarsals were involved. In 27 cases, more than one bone in the tarsus was affected. A history of trauma was obtained in 17 cases, and in 11 cases a positive family history of tuberculosis was found. Other tuberculous foci were present in 20 cases (48 per cent). The age at onset of symptoms varied from ten months to seventy years, with an average of nineteen and a half years. The average age on admission was twenty-four years.

Thirty-seven cases were followed from five months to fourteen and a half years, an average of seven years after discharge from the sanatorium. Three cases could not be followed. Two patients died while in the sanatorium.

Proved cases in adults. Seventeen patients were in this group. Among these, there were 3 deaths: 1 was due to amyloid disease, 1 to a tuberculous spine and tuberculous nephritis, and 1 to postoperative complications in a patient seventy-one years old. Seven patients were treated by amputation, two weeks to two and a half years after admission, and in an additional case an amputation was performed a year after discharge. Of the amputated cases, 2 patients died, and in the remaining 6 cases the stump is well healed and the end result is satisfactory. An amputation was done in 4 cases that had previously received less radical surgical treatment. Conservative treatment only was carried out in 5 cases, and there were good results in 2, poor results in 2, and death (from tuberculous spine and tuberculous nephritis) in 1. Curettage, not followed by any more radical procedure, was successfully performed in 3 cases. A satisfactory arthrodesis, no graft being used, was performed in 1 case.

Unproved cases in adults. Four cases were found in this group and no deaths. In each case, several tarsal bones were involved: astragalus twice, calcaneus once, navicular twice, cuneiforms three times, and cuboid once. Three cases were treated conservatively, with good results in 2. A satisfactory arthrodesis was done in 1 case a month after admission.

Proved cases in children. There were 8 cases and no deaths in this group. In 6 cases, the end results were good, and in the remaining 2, the end results were fair. In 3 cases, treatment consisted largely of plaster immobilization. In 4 cases, curettage was done, but in 3 of these, the disease was apparently localized to a single bone. An arthrodesis was done in only 1 case.

Unproved cases in children. There were 10 patients in this group, all of whom were adequately followed. One of these children had curettage nine months before admission, and an amputation three months before admission. In another case, a biopsy was done. The remaining 8 patients were treated conservatively, with satisfactory end results in every case. There were no deaths in any of these 10 cases.

DISCUSSION

Tuberculosis of the ankle joint in an adult, whether it is proved pathologically or diagnosed on the basis of clinical and roentgenologic evi-

dence, is a fairly serious condition and is associated with a mortality of over 50 per cent. Of the 24 adult patients in this study, 13 died, 11 of some other tuberculous focus, such as a pulmonary one. The results of prolonged conservative treatment and immobilization are poor, and the end results of arthrodesis are equally bad. Midcalf amputation after a short period of hospitalization offers the best hope for a permanent and rapid "cure." Besides, more attention must be given to extraosseous foci, such as the lungs, and the patients should be watched carefully for the development of activity in what may appear to be arrested lesions.

In children, the prognosis of ankle-joint tuberculosis is better. The children in this study were followed for an average period of five years and eight months, as compared with an average follow-up of five years and ten months for the adults with ankle-joint disease. Of a total of 20 cases in children (12 proved, 8 unproved), there were only 4 deaths. Three patients died of tuberculous meningitis, but these 3 were treated by plaster immobilization and no operation was performed that might account for the metastatic spread of the disease. The fourth death was in a patient who had tuberculosis of the spine, wrist and lymph nodes, in addition to the ankle, and an amputation was performed as a possible lifesaving measure. In children, conservative treatment may be carried out safely for longer periods than in adults, with expectations of satisfactory results. An arthrodesis or erosion can safely be done sometimes in other cases, and in a few, amputation offers the only hope of a good end result.

Tuberculosis of the tarsal and metatarsal bones must be considered a different disease from ankle tuberculosis. The mortality of foot tuberculosis in adults was 14 per cent, as compared with 54 per cent for ankle tuberculosis in adults. Ankle-joint tuberculosis in children had a mortality of 25 per cent, as compared with no deaths for tuberculosis of the foot in children. It is apparent that tuberculosis of the foot is a relatively benign disease, as compared with tuberculosis of the ankle.

Adults with tuberculosis of the foot were treated sooner or later by amputation in 8 out of 21 cases. Fifty per cent of the patients with amputation had had an adequate preliminary trial of sanatorium treatment and more conservative surgery. In 5 additional cases, conservative surgical measures gave satisfactory end results. There were only 4 good end results, however, in 8 patients treated only by bed rest and immobilization. Thus, a short trial of conservative treatment should be given to an adult with tuberculosis of the foot. If this fails, surgery less radical than amputation

offers about a 50 per cent chance of success. Amputation, however, should not be withheld until it is demanded as a last resort.

In 18 cases of tuberculosis of the foot in childhood, there were no deaths. Even in cases in which the foot appears angry, swollen and ridged with sinuses, prolonged conservative treatment must first be given a fair trial. Prolonged immobilization and bed rest (as in a sanatorium) offer the best chance for permanent cure. In 11 of 18 cases, conservative treatment gave good end results. Curettage and arthrodesis are usually unnecessary, but if the disease is apparently localized to a single bone, such as a metatarsal, curettage may be successfully performed.

SUMMARY

Tuberculosis of the ankle joint is a serious complication of pulmonary or other tuberculous lesions and was associated with an eventual mortality, from some form of tuberculosis, of 54 per cent in adults and 20 per cent in children in a series followed for an average period of six years after discharge from a sanatorium.

In the treatment of ankle-joint tuberculosis in adults, amputation should not be unduly postponed; in children, about 50 per cent good end results were obtained with sanatorium treatment and immobilization. In a few others, arthrodesis was successfully performed, but some patients required amputation.

Tarsal and metatarsal tuberculosis is a comparatively benign disease, in contrast to ankle-joint tuberculosis. In adults, it was associated with an eventual mortality of only 14 per cent from some form of tuberculosis and no mortality in children after an average period of seven years' observation.

In adults, about two fifths of the cases of foot tuberculosis required amputation, but a longer trial of conservative treatment can be more safely undertaken than in ankle disease. Conservative treatment in children yielded good results in about 60 per cent of the cases, and other simple surgical procedures, such as curettage, were satisfactory. Arthrodesis or amputation was only rarely necessary.

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ALCOHOL AND CEREBRAL VASODILATATION

JULIUS LOMAN, MD, AND ABRAHAM MYERSON, MD†

BOSTON

THE potential clinical usefulness of an efficacious cerebral vasodilator drug is obvious. In cerebral thrombosis, for example, an increase in cerebral blood flow, if brought into play quickly enough after the onset of the vascular accident, may establish adequate collateral circulation in the area involved and diminish the full effects of the developing infarct. Since irreversible changes in brain tissue take place rapidly following a vascular insult, the administration of a vasodilator several hours later is probably of much less therapeutic value. It is possible, however, that the vasodilator, if administered regularly, may prevent further symptoms from developing in such a disease as multiple sclerosis, in which the lesions are considered to be secondary to vascular thromboses. This therapeutic approach has been used by Moore,¹ who reports improvement in cases of multiple sclerosis following the use of niacin (nicotinic acid).

AVAILABLE METHODS

Visualization of Pial Vessels

This procedure is feasible only in animals. Changes in the pial circulation probably, though not necessarily, indicate similar changes in the deeper cerebral circulation. The pial vessels, however, may be much more sensitive than the intracerebral vessels to changes in diameter.

Measurement of Oxygen Uptake by Brain

A change in the arteriovenous difference in oxygen may be due either to actual alterations in cell metabolism or blood flow or to a combination of these factors. For example, ether produces a marked decrease in oxygen uptake by the brain through a profound narcotic effect on the cells of the brain and possibly, in some degree, through an increase in cerebral flow.² If the

metabolic factor can be excluded, a definite change in arteriovenous difference in oxygen is most probably a reflection of altered blood flow in the cerebrovascular bed. Mere dilatation of the larger vessels on the surface of the brain and in the meninges may result in little change in arteriovenous difference in oxygen.

Measurement of Cerebral Blood Flow

Qualitative method. In man, a change in intracranial blood flow may be recorded by the thermoelectric method of Gibbs,³ in which alterations in blood flow are measured in the internal jugular vein at a point where this vessel immediately leaves the skull and is fixed in diameter.

Quantitative method. Recently, a quantitative method for measuring changes in cerebral blood flow has been devised by Ferris.⁴ This procedure makes use of the fact that the intracranial cavity is a natural plethysmograph. When one halts the outflow of blood from the cranial cavity by inflating a cuff about the neck, the rate of outflow of cerebrospinal fluid through the spinal needle is considered to equal the rate of inflow of blood into the cranial cavity.

Measurement of Cerebrospinal Fluid Pressure

This indirect method does not give specific information regarding alterations of flow in the cerebrovascular bed. Changes in the cerebrospinal fluid pressure may indicate changes only in the pial circulation. When, however, lumbar puncture is performed in conjunction with the determination of arteriovenous differences in oxygen, the information obtained may allow more definite conclusions concerning changes in cerebral blood flow. If, for example, niacin produces an significant increase in spinal fluid pressure and a slight decrease in the arteriovenous difference of oxygen, the assumption that the drug is a relatively weak cerebral vasodilator is probably correct (Loman, Rinkel and Myerson).⁵ Again, if after the intravenous administration of sodium amytal, a diminished uptake in cerebral oxygen is associated

†From the Division of Psychiatric Research, Boston State Hospital. This study was aided by a grant from the Commonwealth of Massachusetts. Assistant professor of neurology Tufts College Medical School, research assistant Boston State Hospital, visiting neurologist, Beilinson Hospital, Boston.

Technical professor of psychiatry Harvard Medical School, professor of neurology, Tufts College Medical School, director of research Boston State Hospital.

ed with an unaltered spinal-fluid pressure, the change is probably correctly ascribed to a diminished cerebral metabolism rather than to a variation in cerebral blood flow.² Practically conclusive evidence that this interpretation is correct is obtained by the blood-flow method of Gibbs (Loman and Myerson⁶).

Changes in Caliber of Retinal Vessels

The retinal vessels are outgrowths of the cerebral vessels and are enclosed in a container analo-

of alcohol in physiologic saline solution intravenously, so that they received from 50 to 85 cc. of absolute alcohol. The alcohol was administered slowly for ten to fifteen minutes. All the subjects manifested various degrees of intoxication within a short time after the administration of the drug: drowsiness, silly laughter, talkativeness, euphoria and muscular inco-ordination. Blood was collected from the brachial artery and from the internal jugular vein before the administration of the alcohol and at the height of the alco-

TABLE 1. Arteriojugular Differences in Oxygen Content following Intravenous Administration of Alcohol.

EXPERIMENT No.	DOSE OF ABSOLUTE ALCOHOL cc.	ARTERIOJUGULAR OXYGEN DIFFERENCE		CONDITION OF PATIENT
		BEFORE INJECTION	AT HEIGHT OF REACTION	
		vol. per cent	vol. per cent	
1	50	10.3	6.9	Moderate drowsiness; silly laughter; thick speech.
2	50	6.3	5.5	Slight to moderate drowsiness; pallor and nausea.
3	65	7.0	8.0	Slight to moderate drowsiness; speech very thick.
4	75	5.2	6.7	Slight to moderate drowsiness; continuous innumbling; speech thick.
5	85	6.3	3.8	Unconsciousness; pallor and nausea.
6	80	6.7	6.1	Slight drowsiness
7	80	5.3	5.2	Outbursts of laughter; slight drowsiness; slight pallor.
8	75	4.7	4.0	Euphoria and laughter; no drowsiness.
9	70	6.4	5.7	Slight to moderate drowsiness
10	60	4.9	5.5	Talkativeness; slight drowsiness.

gous to the intracranial cavity. Changes in the diameter of the retinal vessels may indicate similar changes in the caliber of the pial vessels but not necessarily of the intracerebral vessels.

Changes in Velocity of Blood Flow

Alterations in velocity do not necessarily indicate actual changes in blood-volume flow. Since absolutely definite conclusions regarding changes in cerebral blood flow cannot be made in the absence of direct visualization of the cerebrovascular bed, conclusions regarding alterations in flow should be open to some doubt unless data obtained from the various methods coincide.

Because one of the effects of alcohol is flushing, its possible clinical usefulness as a cerebral vasodilator became apparent. Thomas⁷ observed in cats that pial arteries increase in diameter following both the intravenous administration of alcohol and the direct application of the chemical to these vessels. Direct blood-flow measurements showed similar changes. Such effects, however, were noted to be transient, lasting about fifteen minutes. Goldfarb, Bowman and Wortis⁸ found a diminished arteriojugular difference in oxygen in patients admitted to the hospital in a state of alcoholic intoxication. These authors explained the decreased uptake in oxygen on the basis of a decrease in cerebral metabolism rather than on a basis of an alteration in cerebral blood flow.

METHOD USED

In the present experiments, 10 subjects with dementia praecox in good physical health were studied. They were given a 25 per cent solution

of alcohol in physiologic saline solution intravenously, so that they received from 50 to 85 cc. of absolute alcohol. The alcohol was administered slowly for ten to fifteen minutes. All the subjects manifested various degrees of intoxication within a short time after the administration of the drug: drowsiness, silly laughter, talkativeness, euphoria and muscular inco-ordination. Blood was collected from the brachial artery and from the internal jugular vein before the administration of the alcohol and at the height of the alco-

RESULTS

Oxygen uptake. In only 2 (Cases 1 and 5) of the 10 cases was there a significant decrease in oxygen uptake by the brain following the administration of the alcohol (Table 1); one of these subjects was moderately drowsy, and the other was narcotized to the point of sleep. The other 8 exhibited slight to moderate drowsiness.

Sugar content. The uptake of this substance was not significantly altered during the period of alcoholic intoxication.

Cerebrospinal-fluid pressure. In none of the 4 cases in which this test was performed was there any significant change in pressure.

DISCUSSION

The dose of alcohol used in the present experiments may be considered adequate to test the vasodilating action of the drug. Larger amounts would probably be too depressant to the brain to offset any possible cerebral vasodilatation. It is likely that any diminution of oxygen uptake by the brain following the administration of alcohol is related to a diminished cerebral metabolism rather than to cerebral vasodilatation. In the 2 cases in

which a diminished oxygen uptake occurred, the drowsiness was moderate to marked. The fact that the cerebrospinal-fluid pressure was unaltered during the administration of the alcohol also indicates the inefficacy of alcohol as a cerebral vasodilator. Although the lack of a significant change in glucose uptake by the brain during the alcohol intoxication suggests a change neither in cerebral metabolism nor in cerebral blood flow, it is probable that a change in uptake of this metabolite is an unreliable index of alteration in cerebral blood flow.

Since alcohol acts as a cerebral depressant, it appears not to have any especial advantage over other vasodilators. Several other drugs not having a depressing effect on the brain are known to have a cerebral vasodilating action. Such drugs include carbon dioxide, histamine, the nitrites, acetylcholine and niacin. They all, however, have a transient vasodilating action, and in effective dosage some of them are apt to have undesirable side effects.

It is suggested that effective and prolonged cerebral vasodilatation, with the elimination of undesirable side effects, may be accomplished by slow continuous intravenous infusion. For this purpose, niacin and histamine are probably more desirable than the nitrites and acetylcholine. A mixture of 10 per cent carbon dioxide and 90 per cent oxygen also merits more frequent trial, since carbon dioxide has a specific cerebral vasodilating action (Lennox and Gibbs⁹).

SUMMARY AND CONCLUSIONS

Alcohol was administered by intravenous route to 10 subjects in doses sufficient to produce definite

signs of intoxication. Oxygen and glucose uptakes between the arterial and internal jugular venous blood were compared before and at the height of the intoxication. The cerebrospinal fluid pressure was measured in 4 subjects.

In only 2 cases was there a noteworthy decrease in oxygen uptake by the brain. This change is interpreted as a decrease in cerebral metabolism, rather than as an increase in cerebral blood flow. The uptake of glucose by the brain was not significantly altered, nor was there a noteworthy change in the cerebrospinal fluid pressure.

These data indicate that alcohol is not an efficacious cerebral vasodilator. It is suggested that other drugs, particularly niacin (nicotinic acid) and histamine, may be of value as cerebral vasodilators if given by slow intravenous administration in dilute concentrations. A mixture of 10 per cent carbon dioxide and 90 per cent oxygen is also worthy of more frequent trial in cerebral conditions in which an increased blood flow seems desirable.

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MEDICAL PROGRESS

THE TREATMENT OF RHEUMATOID ARTHRITIS*

CHARLES L. SHORT, M.D.,† AND WALTER BAUER, M.D.‡

BOSTON

THE cause of rheumatoid arthritis remains unknown. Although many theories (infectious, metabolic, endocrine, circulatory and neurogenic) have been proposed, no one of them has been generally accepted. This disease presents a variety of clinical forms and pursues no single pattern of development. It must be regarded as a distinct disease entity that can readily be recognized. Space does not permit more than a listing of the outstanding features that distinguish rheumatoid arthritis from other forms of joint disease. It is essential to realize that one is dealing with a generalized disease with well-marked constitutional manifestations that are not merely secondary to the articular lesions. Females are more commonly affected than males, except in cases in which the spine is involved. The onset is not limited to any age group and may occur from infancy to senility. Constitutional symptoms often precede the appearance of objective joint signs, and it is thus possible to surmise the diagnosis in what may be termed a prodromal stage. The type of onset ranges from the insidious to the explosive, with endless variations between. In many cases, the initial complaints are fatigue, exhaustion, lassitude, loss of weight and symptoms referable to the nervous system and the vasomotor apparatus. Both large and small joints are affected, at first perhaps in a migratory fashion but later with unrelenting persistence. Examination of the joints reveals no early findings that are specifically different from those of other forms of arthritis. The signs of inflammation, usually mild and often accompanied by effusion, almost always precede the development of limitation of motion and deformity. More important is the symmetrical, polyarticular distribution of the arthritis, although involvement of one or a few joints is not uncommon in early stages. Muscular weakness and atrophy are prominent, and inflammation of extra-articular fibrous tissue

is almost invariably present, subcutaneous nodules forming a characteristic part of the clinical picture in about 20 per cent of the cases. Involvement of other organs of the body is evidenced in certain cases by cold, clammy hands and feet, atrophy and pigmentation of the skin, lymphadenopathy and splenomegaly, pericarditis and pleuritis, and ocular changes including uveitis and scleritis. The course of the disease is all too often one of steady or intermittent progression, although complete or nearly complete remissions are not unusual at first, and certain patients recover without significant residual disability.

Laboratory studies, although not of diagnostic help, may aid in the determination of the severity of the disease. The sedimentation rate of the red cells and the Schilling or filament-nonfilament counts are useful in following the course of the disease, but only occasionally in differential diagnosis. In approximately 50 per cent of the cases, the serums of patients with rheumatoid arthritis agglutinate strains of hemolytic streptococci of Lancefield Group A in a characteristic manner. In such cases, a positive test is of value in distinguishing rheumatoid arthritis from other forms of arthritis in which positive agglutinations are encountered only rarely. Unfortunately, the test is rarely positive in patients having the disease less than one year. The antistreptolysin and antifibrinolysin titers in rheumatoid-arthritis serums are not characteristic, whereas rheumatic-fever serums usually show elevated values. Biopsy of subcutaneous nodules is frequently of aid in differentiating the former disease from the latter. Examination of synovial fluid is helpful in ruling out traumatic arthritis, degenerative joint disease and the specific infectious arthritides. A hypochromic anemia is often found in severe cases. The white-cell count varies considerably. In most cases, it is within normal limits or only slightly elevated. In the acute and active stages, counts of 12,000 to 20,000 may be observed, whereas in long-standing, chronic cases a definite leukopenia may develop.

Roentgenograms in joint disease must always be interpreted in the light of the duration, severity and articular distribution. With the aid of such facts, accurate roentgenologic diagnosis of rheumatoid arthritis is usually possible. The characteristic features include soft-tissue swelling, effusion,

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From the Medical Clinic, Massachusetts General Hospital, the Department of Medicine, Harvard Medical School, and the Massachusetts Department of Public Health.

†Assistant physician, Massachusetts General Hospital; instructor in medicine, Harvard Medical School.

‡Physician, Massachusetts General Hospital; associate professor in medicine, Harvard Medical School.

systemic decalcification of bone, loss of bony substance in "punched-out" areas, narrowing or even obliteration of the joint space, marginal erosion and, finally, subluxation and gross bony destruction. No single feature mentioned constitutes a diagnostic criterion, and it has been truly said that the picture differs from that of specific infectious arthritis largely in speed of progression.

Because of limitation of space, points helpful in differential diagnosis are not considered at length. Those interested in this aspect of the subject are referred to a previous report.¹ However, it should be emphasized that although rheumatic fever in its classic form is readily recognized, the acute type of rheumatoid arthritis, as well as rheumatic fever tending toward long-continued joint involvement, may render accurate diagnosis extremely difficult. At the present state of knowledge, it must be assumed that the development of endocarditis signifies the coincidental presence of rheumatic fever. A migratory arthritis, tending to complete remission and restitution of joint function, is, of course, strongly in favor of rheumatic fever. Erythematous skin lesions, electrocardiographic changes and rapid response to salicylization are also helpful in the decision for this diagnosis. The subcutaneous nodules in rheumatic fever tend to appear in crops, are transitory, and usually disappear before reaching the size of those found in rheumatoid arthritis; as previously stated, they can be differentiated at biopsy, but only by a pathologist experienced in this field.² In many cases, final decision between the two diseases must be left to the passage of time. Fortunately, nothing is lost by reservation of judgment, since the treatment is essentially the same for both diseases in this stage. The physician should not be afraid to admit the necessity for the passage of time to give the answer, since the patient is only too glad to learn that there is a reasonable doubt that he is suffering from a potentially crippling disease. It should be emphasized that the diagnosis of rheumatoid arthritis should never be made without due consideration and that the disease deserves the same respect and care accorded pulmonary tuberculosis and cancer.

TREATMENT

Because the cause of rheumatoid arthritis is unknown, there is no specific therapy directed toward an etiologic agent. The evidence at hand points to an unrecognized infectious origin. Measures to increase the patient's resistance and place him in the best general health, in addition to proper handling of the inflamed articulations to promote healing and preserve function, are therefore in order. Once the diagnosis has been made, the patient should know what is ahead of him

and should be informed that there is no easy and rapid road toward arrest of the disease. He should also be made acquainted with the natural course of rheumatoid arthritis, so that he will not relax his precautions as a result of a remission or become overly depressed from a relapse. An optimistic, courageous, resourceful attitude is a requisite for the physician who would successfully treat this disease and not see some of his patients wander off to patent remedies and quacks. He must even at times compromise with his intellectual honesty and employ methods of doubtful value, to hold the patient to the pursuit of a few simple measures of proved worth. Thus, the use of vaccines or other parenteral medication of unproved value, combined with generous measures of suggestion, may tide the patient over a discouraging period when the disease seems to be at a standstill or progressing in spite of all efforts.

Treatment varies, of course, according to the stage in which the patient is seen. In the initial, acute attack, there is a very good chance of remission or even arrest of the disease. Continued rest and care after symptoms have apparently subsided are well worth the time and money expended. In patients in whom the disease is well established but relatively quiescent, the physician can temporize and attempt to adapt the scheme of treatment to the patient's occupation and habits, being careful, however, to resume restrictions at the first definite sign of an exacerbation. Instruction should always be definite and detailed, preferably written out. The possibility of a remission when things look darkest should never be lost sight of. The startling freedom from symptoms gained from intercurrent hepatic jaundice or pregnancy points out that the process is not irreversible and that the long-awaited specific method of treatment may yet come to light. Most students of the disease are of the opinion that the treatment of rheumatoid arthritis can be divided as follows: measures of proved value; and measures frequently employed but of questionable value.

Measures of Proved Value

It is agreed that general measures—including rest of the whole patient and of the joints, along with an attempt to preserve, so far as possible, the function of the articulations and muscles—form the backbone of the treatment of rheumatoid arthritis. Realizing the difficulty of evaluating therapeutic claims, one should never be too dogmatic in stressing the value of any single measure. Hospitalization is always of benefit when the patient is first seen, not only for the more adequate care of severe cases but also for diagnostic studies and observation if needed, to teach the patient principles and methods that can later be pur-

sued at home and to provide orthopedic apparatus. How long such treatment should be continued will depend on individual factors such as the course and severity of the disease, the patient's financial resources and the suitability of conditions for care at home.

Rest. Complete rest in bed is essential in certain forms of the disease. The first is made up of acute febrile cases with severely inflamed joints and often resembling a specific infectious arthritis or rheumatic fever. Other forms include rapidly progressive cases, although the patient may be afebrile and the joints not acutely inflamed, patients with marked constitutional manifestations and, finally, those whose weight-bearing joints are so inflamed or deformed as to make walking unwise. The duration of bed rest, of course, depends on the patient's response. In general, this situation is very much like that in pulmonary tuberculosis in which, to ensure against reactivation of the disease, rest must be prolonged even after the patient has started to improve. Similarly, the process of getting up must be gradual and guarded. Sitting on the edge of the bed or in a chair for ten to fifteen minutes is all that should be allowed at first, with increases slowly granted and gauged according to the patient's response. The physician must outline carefully the extent and duration of bed rest as soon as he has been able to estimate the necessary program, with the provision that unforeseen changes may force an alteration in the plan.

The patients with milder cases who do not need bed rest when first seen, and those who have improved beyond that stage should continue to obtain more rest for an indefinite time. This may vary from ten to twelve hours in bed each night, in addition to an afternoon nap, to bed rest from eighteen to twenty hours out of the twenty-four. In such patients, the symptom of fatigue is as important a guide as the state of the joints. In other words, fatigue is a condition to be avoided at all cost—a principle to be learned and followed by the patient himself. If the patient is confined to bed for a long period at home, a hospital bed with an adjustable spring and mattress is well worth the rental or purchase price to both patient and attendant. If the lower extremities are involved, a cradle or footboard is often necessary. The need for nursing care, of course, varies with the individual case. A practical or household nurse usually suffices if carefully directed by the doctor. If nursing care is unavailable or unnecessary, a responsible member of the household should be chosen to act for the physician to see that the course of the treatment is faithfully carried out. Finally, rest can be aided

materially by the judicious use of analgesics and hypnotics. Their use is described below.

Treatment of joints. Rest of the involved joints promotes healing and is often essential to the comfort of the patient. Weight bearing should not be allowed on acutely inflamed joints or those with heat or atrophied muscles, or both, or fixed in poor weight-bearing line. Once weight bearing is allowed, protection by means of bandages, splints or crutches is usually necessary. The production of subcutaneous nodules in points exposed to irritation furnishes an indication that rheumatoid tissue is affected adversely by trauma. Rest of joints also affords relief from muscle spasm and tension and allows for a decrease in swelling. The use of splints or casts further allows the joint inflammation to subside, keeps the joint in an optimal position for function and protects against the deforming influences of muscle spasm and gravity.

Prevention and correction of deformities are vital in the treatment of this disease. In many patients with arthritis, severe deformities and contractures occur in joints that have received inadequate splinting. The physician must be alert to this possibility and forestall it by careful splinting of the affected joints in the position of optimal function. Molded plaster splints or bivalved plaster casts are the most comfortable and efficient devices for the feet and knees. The plaster should be shaped so that the foot is supported at a right angle to the leg, and the arch carefully molded, with additional support just behind the metatarsal heads so that the toes are kept straight. The plaster should extend beyond the toes, and a crossbar of wood should be incorporated at the heel to prevent outward rotation deformity of the hip. It should extend upward to the gluteal fold.

Although continuous use of these protective appliances is necessary at first, they may later be used only at night or for certain periods during the day. When casts are employed, they should be bivalved after the first few days so that the joints may be given physical therapy (exercises, massage and so forth). From the very beginning, a determined effort must be made by physician and patient to preserve articular function. Even if the joints are acutely inflamed, a gentle, guided and supported movement or two is possible each day and is immeasurably helpful in the prevention of adhesions and ankylosis. Later on, systematic active exercises such as are used in anterior poliomyelitis should be performed several times daily, limited only by fatigue and pain, not during but persisting after the exercises. Regular exercises probably aid in the absorption of exudates and encourage the will and discipline of the patient. Along with such exercises of the joints, the patient should be

taught to assume a supine position, with the bed flat, for increasing periods up to several hours a day. At this time, breathing and postural exercises can be done. Even if experienced in the treatment of rheumatoid arthritis, the physician will do well to seek the advice and aid of the orthopedist both at the beginning and at regular intervals in the course of the treatment of any patient whose joints are severely involved.

Physical therapy cannot be dispensed with in the treatment of rheumatoid arthritis. The knowledge that heat, exercise and massage are beneficial in the treatment of this disease probably antedates all recorded medical teaching. Unfortunately, there is still no adequate knowledge of the mechanism by which these measures give relief, and one must prescribe physical therapy largely according to its effect. The joints and periarticular structures of most patients with rheumatoid arthritis are less painful and move more freely after the application of heat. A few exceptions are found in patients with acute, severely inflamed joints and in the not uncommonly encountered persons whose joints are more painful when heat is applied. For the first group, simple fixation should be used until the inflammation subsides; for the second, the patient's word should be immediately accepted and heat withheld or even a trial made with cold applications. There is no scientific and little clinical evidence that any form of heat is superior. In the hospital, local diathermy or carefully applied hot packs may be serviceable; in the home, an inexpensive electric baker or an electric pad can be employed. The duration of the application of heat should not cause tiring or discomfort. Several brief applications a day are better than one more prolonged. In general, a visible reaction should be effected, with reddening and sweating of the overlying skin. If excessive fluid or salts are lost in the sweat, with a weakening effect, water and sodium chloride must be supplied.

When multiple joints are involved, immersion of the patient in a hot bath or under a hot shower often relieves symptoms. This form of treatment is not indicated in debilitated patients or in those with too active an arthritis to permit movement to a tub or shower. The length of the patient's stay in the water should be gradually increased up to a maximum of half an hour. The bath may be given every day if well tolerated, the most effective time being the morning. A safe bath temperature to begin with is 100°F., but this can often be increased as time goes on. If the patient complains of perspiration accompanied by weakness during this course of treatment, extra sodium chloride must be supplied. Immersion of the ex-

trémities in contrast baths (hot water followed by cold) is of value in certain cases; these are usually cases with less advanced changes, but again the decision must be made on the response of the patient. If increased pain is caused by contrast baths, heat alone should be applied. The best schedule to follow is: immersion in hot water for six minutes, immersion in cold water for four minutes, immersion in hot water for six minutes and so on, for a total of seven times, four hot and three cold.

Pools similar to those employed in the aftercare of poliomyelitis to allow exercise of the legs without weight bearing are of value if available. Massage given in the pool should be gentle and applied to muscles rather than to joints.

Fever therapy is often beneficial for patients in good general condition in whom the disease is stationary or gradually progressive. No dramatic, curative results can be expected, but the patient's symptoms may be temporarily improved and his determination thus strengthened. In a few cases, the gain following fever therapy may be held and even increased in the course of general treatment. The various methods of providing fever can be used according to their availability.

No specific effect of sunlight on the course of rheumatoid arthritis has been demonstrated, but its use in control dosage may aid the patient's appetite and sense of well-being. If the patient can be exposed to the sun fairly regularly, vitamin D preparations can be dispensed with. Excessive exposure to sunlight should be avoided.

Surgery and manipulation of the joints are often indicated in the treatment of rheumatoid arthritis. With proper selection of cases and procedure, and with close attention to operative detail and follow-up care, marked improvement in joint function may be expected from certain orthopedic operations. However, there are many pitfalls to be avoided, and it is only after the most careful study of the individual case and under skilled supervision that operative intervention is to be undertaken. It is impossible to give more than a list of the types of procedures available, with a few of their indications.

Whenever possible, deformities should be corrected by the simplest method that will suffice. Daily gentle stretching of quiescent but stiff joints is the safest procedure of mobilization. In many cases, one may safely straighten a flexed knee by applying a cast in maximal correction, bivalving the cast and, after a few days to a week of physical therapy, applying another cast. With each change of plaster, it is usually possible to gain further correction until the knee deformity is completely overcome. Although this method is slow,

it is very comfortable and avoids many dangers of the more forceful methods. Acute deformed joints may often be put in correct position by gentle manipulation under light general anesthesia. The new position should be maintained by proper splinting or a carefully applied cast that is not disturbed until the reaction from the manipulation has subsided. Wedging casts are often employed for the correction of knee-flexion deformity but are contraindicated if there is evidence of an acutely inflamed synovial lining or posterior subluxation of the tibia on the femur. Extreme care is necessary if pressure sores are to be avoided. Adhesive or skeletal traction, often combined with posterior capsuloplasty, may be resorted to in the severer and more intractable knee-flexion deformities. Synovectomy is definitely contraindicated in the acute phase of rheumatoid arthritis, but certain knees, which under prolonged conservative care have failed to become quiescent, are much improved by a subtotal removal of the synovial membrane.

A joint that is so destroyed by the pathologic process that all useful motion has been lost and yet remains painful presents a problem in selection of operative procedure. The choice rests between arthrodesis and arthroplasty. The former has the advantage of practically assuring a pain-free joint, and the operation may be performed while the disease is still active; the wrists, shoulders, hips, knees and ankles are most frequently selected for arthrodesis. Arthroplasty—that is, the restoration of motion in an ankylosed joint by operative means—should be undertaken only after the most careful consideration of many factors. The joint and all other joints must be in a quiescent phase. If there is a recrudescence of the disease, the operation usually fails. Since the postoperative care is prolonged and often painful, the patient should be co-operative and not hypersensitive to pain. The elbow, interphalangeal joints of the fingers, the hip and the knee are the most favorable joints for arthroplasty. Osteotomy may be used occasionally to improve the position of an ankylosed joint.

Diet. The patient with rheumatoid arthritis has long been subject to varying forms of dietary restrictions. Because of the age-old confusion of the disease with gout, he may still be deprived of the vital body-building substances contained in meat. The citrus fruits, which are the best known source of vitamin C, should not be deleted from the dietary of the patient with rheumatoid arthritis because of their supposed "acid-producing qualities." A low-calorie diet with carbohydrates reduced to a minimum should not be prescribed for a patient whose weight and energy are below par. No ex-

perimental evidence adequately supports the majority of the diets that have been used in the past. Carefully controlled clinical studies³ have shown benefit rather than harm from the employment of diets high in proteins and carbohydrates and containing large amounts of citrus fruits. No one food or class of foods needs to be restricted in the diet of a patient with rheumatoid arthritis.

There is no proof that the etiology of this disease lies in a dietary deficiency. Clinical experience has repeatedly shown that therapy based on the supplying of one or more dietary factors in normal or excessive quantities offers no hope of success. Nevertheless, a surprising amount of improvement in energy and nutrition may often be gained from dietary therapy alone. On what must be admitted are for the present largely empirical grounds, we believe that a patient with rheumatoid arthritis should receive a diet that is more than adequate in every respect, with the calories adjusted to the patient's energy requirements and weight. Since weight loss is common, a high-calorie diet is usually required. To aid in combating the diffuse and local bone atrophy that is frequently present, the diet should be abundant in calcium and phosphorus, with sufficient additional vitamin D in concentrated form to ensure complete absorption of these minerals from the gastrointestinal tract. For the treatment or the prophylaxis of the hypochromic anemia that may accompany severe cases, a sufficient supply of iron and meat (especially liver) must be prescribed. Provision should also be made for an ample intake of the other important vitamins. Carbohydrates need be restricted only if the patient is overweight or if such restriction is necessary to provide for an adequate intake of more essential factors. Such a diet supplies a sufficient amount of roughage, which may require curtailment if the patient possesses an overirritable bowel. In summary, the diet of the patient with rheumatoid arthritis should contain as much fresh fruit and fresh vegetables as possible, at least two glasses of fruit juice or tomato juice, seafood, fowl or meat of any kind and two or three glasses of milk. He should be allowed butter, cream, cheese and eggs as desired. The rest of his diet can be adjusted to his own choice, provided he does not gain too much weight.

Vitamins. As stated above, rheumatoid arthritis does not originate from vitamin deficiency and cannot be cured by the administration of normal or excessive amounts of vitamins. The prescription of concentrated vitamins is warranted only on the basis of securing a well-balanced dietary intake containing optimal amounts of the necessary constituents. For this purpose, but with no

thought of a specific effect, we usually advise the patient to partake of vitamin concentrates in addition to a well rounded diet.

Besides continuing vitamins A and D, cod liver oil in dosage of 2 or 3 ounces (60 to 90 cc) daily is unsurpassed in its ability to put weight on a patient. If a gain in weight is unnecessary or undesirable, or if the patient is unable to take cod liver oil, vitamins A and D may be supplied in concentrated form. Although the decalcification noted in rheumatoid arthritis has not been shown to be secondary to a primary disturbance in calcium and phosphorus metabolism, it seems reasonable not only to supply adequate amounts of these minerals in the diet but also to ensure their absorption from the gastrointestinal tract. Recently, reports have claimed that marked clinical improvement follows the administration of massive doses of vitamin D (150,000 to 1,000,000 U.S.P. units daily). Carefully controlled studies by others⁴ have shown that such dosage does not alter the course of the disease and, in addition, exposes the patient to the discomfort of nausea and vomiting and other toxic manifestations and the dangers of persistent hypercalcemia. For these reasons, we do not recommend the use of vitamin D preparations in amounts above the usual therapeutic dosage (5000 to 10,000 U.S.P. units daily).

In addition to its role as a part of the normal human dietary, the vitamin B complex may be useful in promoting appetite and normal functioning of the gastrointestinal tract. Occasionally, when prescribed as brewer's yeast or yeast concentrate tablets, this form of medication defeats its own purpose and causes digestive upsets. In such cases, thiamine chloride may be prescribed alone in dosage of 1 to 3 mg daily, or with the addition of riboflavin and niacin (nicotinic acid).

Recent studies have shown that many patients with rheumatoid arthritis have a subnormal level of vitamin C in the blood. Furthermore, such patients have a greater demand for vitamin C and can tolerate a large intake without much loss in the urine. In spite of this interesting therapeutic lead, carefully controlled studies have failed to show improvement in the course of the disease, even though 200 mg or more of vitamin C are administered daily for as long as eight months. For patients who are able to take 8 ounces of orange juice daily, extra amounts of vitamin C in crystalline form appear to be superfluous.

Climate That the symptoms of rheumatoid arthritis may be enhanced by dampness or changes in weather is known to the man in the street as well as to the student of the disease. There is little proof, however, that climatic conditions and dampness bear a direct etiologic relation to the

onset of the disease. Rheumatoid arthritis is said to be rare in the tropics, but further work in geographic pathology is necessary to establish this point. Patients who migrate to a warm, dry climate usually do not improve unless the disease is actively supervised and treated. It is reasonable that a patient with rheumatoid arthritis, if only for his own comfort, should avoid chilling and dampness and should wear warm outer and inner clothing in the winter season of the temperate zone. Whether or not he should move to a warm, dry climate is another question. Such a move should certainly not be made at great financial sacrifice and should not involve giving up the possibility of a gainful occupation. A period of at least six to twelve months must be devoted to the project to make it worth while. A definite arrangement should be made beforehand so that the patient can receive proper treatment and supervision. Most of the advantages from change of climate are probably due to the fact that because the patient has made this radical step, he is willing to go still farther and put himself under sanatorium treatment. A stay in the South may be of great benefit to an occasional patient who will accept regulation and supervision only under the guise of climatotherapy. Although a winter in the South is a pleasant luxury for the patient who can afford it, in most cases the disease must be combated in the patient's own environment.

Foci of infection Irrespective of the claims made by various workers concerning the role of foci of infection in the production of rheumatoid arthritis, most students of the disease agree that it is as great a problem today as before the introduction of the theory of focal infection. A careful and conservative attitude is indicated. The best one can do is to lay down certain principles and indications. If the arthritis follows directly on an infection susceptible to treatment, such as an attack of tonsillitis, focal removal is wise. We have found that such patients bear some liability to exacerbations in the arthritis following subsequent attacks. Focal removal should never be used to the exclusion of valuable general measures or to delay their execution. Expensive combating of the patient for sources of infection is rarely warranted, and consultants' reports must be interpreted and acted on by the doctor in charge of the patient. The evidence is distinctly against the importance of the gall bladder, appendix, bowel (constipation) and male and female genitourinary tracts as foci of infection. Therefore, medical or surgical measures for these regions should be employed only as indicated to improve the general health of a patient without arthritis. The role of dental

infections, especially the pulpless tooth, has probably been exaggerated. Even if infection is demonstrably present, the practitioner may be justified in advising against the extraction of necessary teeth in debilitated patients and thus running the risk of interfering with their nutrition. Advanced cases are rarely benefited by focal removal unless this is essential for their general health. In patients over fifty, the risks of anesthesia and operation must be considered. As is apparent, we have adopted a conservative attitude, which we consider justified at present.

Drug therapy. Like other chronic diseases of unknown origin, rheumatoid arthritis has not suffered from a paucity of remedies of supposed curative value. For our purpose, an exhaustive listing and discussion of drugs of unproved worth is unnecessary and would merely be confusing. We shall, therefore, confine ourselves to drugs of value in the relief of symptoms. The so-called "specific measures" that merit attention either from a certain amount of favorable evidence or from the combined notoriety of enthusiastic clinical reports and extensive advertising will be discussed in a subsequent section.

Relief of pain is of paramount importance in the treatment of rheumatoid arthritis. Pain interferes with rest, sleep, exercise and appetite—all critical factors in recovery. It has been shown that pain decreases peripheral circulation and muscle function, presumably through nervous reflexes. In certain cases, the patient would be reasonably well, so far as articular function or constitutional symptoms are concerned, were it not for the presence of persistent disabling pain. Without denying that measures such as rest, physiotherapy, fixation of joints and even psychotherapy play a major part in lessening pain, in many cases the physician should rightly resort to the use of drugs until the symptoms can be controlled by other methods.

The salicylates rank first for this purpose from the standpoint of both safety and efficacy. Aspirin is usually more effective than sodium salicylate, which, however, is less likely to cause gastric symptoms. The amount used should depend entirely on the patient's response, care being taken, of course, to fall short of toxic manifestations. Many patients need 10 gr. (0.6 gm.) every four hours, and others as much as 15 to 20 gr. (1.0 to 1.3 gm.) every three hours. Since so many patients with rheumatoid arthritis suffer pain and stiffness in the early morning hours and are relatively free later on in the day, the first dose may be given as soon as the patient awakens, followed by another after breakfast. The addition of sodium bicarbonate or the substitution of equal doses of phenacetin often serves to allay gastric disturbances. Phenacetin is also useful in patients who

are not entirely relieved by aspirin. Proprietary preparations, usually with the salicylate radical or aspirin as a basis, have not been found more effective except that they are occasionally better tolerated by the stomach. Although ammonium ortho-iodoxybenzoic acid (Amidoxyl) given intravenously in 1 per cent solution sometimes relieves pain for several days or longer in a stubborn case, this drug must be considered an entirely symptomatic rather than a specific remedy, and care must be taken in its administration to avoid unpleasant reactions. Products containing aminopyrine (Pyramidon) had best be entirely dispensed with if possible on account of the rare but real possibility of a serious or fatal granulocytopenia. The same caution applies to cinchophen and compounds that may cause severe, often fatal, liver damage.

If the salicylates are not entirely effective, codeine in amounts of $\frac{1}{4}$ to 1 gr. (0.017 to 0.067 gm.) may be added to each dose of salicylates. The physician should remember that codeine alone is a much less effective analgesic than in combination with the salicylates. Only occasionally is the use of morphine, pantopon or dilaudid justified. We cannot overemphasize the dangers of addiction in a patient with a chronic disease.

Hypnotics are valuable for patients unable to sleep, unless the insomnia is clearly due to pain. The use of these drugs in rheumatoid arthritis does not differ from that in other conditions, except that special care should be taken to avoid depression the next morning. The combined use of a hypnotic and an analgesic at bedtime is often more effective than either alone. Patients in whom it is suspected that part of the symptoms may be due to emotional causes are benefited by mild continued sedation such as that obtained from phenobarbital, $\frac{1}{4}$ to $\frac{1}{2}$ gr. (0.017 to 0.033 gm.), four times daily.

Novocain block usually gives temporary relief to a painful extremity that fails to respond to other measures. At times, the relief of pain is held, the vicious cycle of pain, muscle spasm and disability apparently being broken by one or two infiltrations with an aqueous solution of 2 per cent novocain above the affected joint. Further trial should be made of this method.

Transfusions. If the anemia present fails to respond to iron in adequate dosage, blood transfusions are needed to bring the hemoglobin and red-cell levels to normal. In addition, transfusions in certain cases apparently may initiate a striking remission. If tried, at least two, of 500 cc. each, should be given.

Psychotherapy. The temporal relation of disturbing environmental factors to the onset and exacerbations of rheumatoid arthritis has long been noticed and recorded in isolated cases.

Recent studies⁵ of an unselected group of patients with rheumatoid arthritis compared with a control group with varicose veins have shown such a relation to exist in a significant number of cases. Without implying that rheumatoid arthritis is of psychogenic origin, we do believe that the physician must recognize the fact that worry, grief and anxiety can be major contributory factors in the progression of this chronic disease. In certain patients, symptoms of undoubtedly functional origin, even classic hysteria, may be superimposed on those due to the arthritis itself. Since pain may be present, apparently out of all proportion to the activity and extent of the disease, the burden of proof should be on the physician to determine that fears and conflicts are responsible for a low threshold of sensitivity. In a few patients, superficial investigation along these lines is revealing and rewarding, the excessive pain being strikingly relieved by the sympathetic listening and encouragement of the physician. In all patients, the initiative, leadership and resourcefulness of the doctor count heavily in whatever success is obtained. A set routine to be carried out according to detailed instructions is valuable from the point of view of suggestion. Equal benefit is obtained by a change in the routine from time to time, both according to the progress of the disease and to maintain the patient's interest and confidence.

Measures Frequently Employed but of Questionable Value

Vaccines. That no theoretical basis exists for the use of vaccine therapy in rheumatoid arthritis rests on two considerations: we are not acquainted with a single disease of known cause in which vaccine treatment is effective; and there can be no specific vaccine for a disease of unknown etiology, and organisms isolated at random from the nasopharynx or stools cannot be deemed specific even with positive skin and complement-fixation reactions.⁶ Since the therapeutic results are negative in carefully controlled series of cases,⁷ one may conclude that there is neither clinical nor theoretical ground for the use of vaccines in rheumatoid arthritis. As mentioned above, there is no objection to their use in patients who are doing badly or standing still, to afford the doctor opportunity to continue with general measures of value and keep the patient under supervision. The same thing applies to the injection of various foreign proteins, including milk and peptone.

The intravenous injection of typhoid vaccine in amounts sufficient to cause a rise in temperature falls under the section on fever therapy.

Sulfur. Recent careful studies⁸ have shown that a primary disturbance in sulfur metabolism is not present in rheumatoid arthritis. Clinical evidence

of benefit from sulfur therapy rests on premature, poorly controlled and overenthusiastic reports.⁹ With the data available at present, sulfur, whether administered by mouth or parenterally, has no place in the treatment of rheumatoid arthritis.

Large doses of vitamin D. As stated above, the administration of excessive doses of vitamin D has no place in the treatment of rheumatoid arthritis. Furthermore, the administration of vitamin D in the amounts advocated by some workers is not without harm to the patient.

Cobra venom. This substance has been successfully used in the treatment of intractable pain due to cancer. Carefully controlled studies in this clinic¹⁰ have shown this form of treatment to be ineffective in relieving the pain of rheumatoid arthritis.

Bee venom. In spite of the advocacy of bee venom by certain workers, the preliminary reports concerning its use have been favorable in only a small percentage of cases. The good results have not as yet been substantiated, and its use is therefore not recommended.

Chaulmoogra oil. There is no indication for the use of chaulmoogra oil in the treatment of rheumatoid arthritis.

Arsenic and iodides. These drugs have long enjoyed an undeserved reputation in the treatment of rheumatoid arthritis, their supposed action being vaguely explained as that of "alteratives."

Endocrine therapy. No endocrine preparation has been shown to exert a specific effect in rheumatoid arthritis. There is no evidence of hypothyroidism in this condition, and treatment with thyroid has been unsuccessful in our hands, even in relieving the vasomotor symptoms by increasing the peripheral circulation.

Although the disease shows a high incidence in women of menopausal age, a direct connection between the menopause and the onset or progress of the disease has not been demonstrated. Replacement therapy with estrogenic material may be used legitimately for relief of distressing menopausal symptoms but not with the hope of altering the arthritis.

Adrenocortical preparations do not help the asthenia so often noted in rheumatoid arthritis, although the pigmentation, low blood pressure and extreme weakness may suggest Addison's disease.

Skeletal decalcification is common in rheumatoid arthritis, but metabolic studies have not shown that this is due to overactivity of the parathyroid glands, and their removal is not indicated.

Gold. Since their introduction by Forestier¹¹ about ten years ago, gold salts have been used extensively in the treatment of rheumatoid arthritis on the Continent and in England. This form of therapy has been slow to gain acceptance in the

United States, largely owing to the dangers of toxicity. Recently, carefully observed series of cases have appeared in the American literature. Writers on the subject have been almost unanimous in stating that although toxic reactions are common and occasionally serious, gold therapy constitutes the most valuable form of treatment known at present for rheumatoid arthritis. Because of the importance of the subject and the limited space available, we shall defer detailed comment on this form of therapy. At present, we are convinced that further experience is necessary before we shall know the therapeutic value of gold in rheumatoid arthritis, to say nothing of how it works to produce its effects. From the figures in the literature and from our own preliminary results,^{12, 13} the case for gold as a specific treatment of rheumatoid arthritis remains unproved. Further work will decide whether this form of therapy merits the acclaim given it by some workers. It is not constantly effective, and it carries a danger of toxicity too great for any but an indispensable drug.

TREATMENT OF RHEUMATOID SPONDYLITIS

Involvement of the spine may precede, accompany or follow rheumatoid arthritis of the peripheral joints. Contrary to the usual sex distribution, the spinal form of the disease is vastly commoner in males. The general treatment outlined for rheumatoid arthritis is equally applicable to this form of spondylitis, which is also called "spondylitis deformans," "spondylitis rhizomelica" and "Strümpell-Marie Arthritis." Removal of the foci of infection is of unproved benefit. If untreated, these patients usually develop severe spinal deformities and, often, hip and knee flexion deformities. As soon as the diagnosis of rheumatoid spondylitis is made, therefore, the physician should devote every effort to keeping the patient's spine in optimal position. The patient should sleep on a firm hair mattress, with fracture boards beneath it, or on a Bradford frame or in a plaster body shell lined with felt. A flexion deformity already present may be corrected slowly by stretching of the dorsal spine over a blanket roll for fifteen-minute periods, three or four times daily. Gentle hyperextension under general anesthesia, repeated at fortnightly intervals if necessary, may be used if other methods fail. As the deformity is reduced, the bed or plaster shell is altered to fit the spinal curves. Deep-breathing exercises should be prescribed and carried out at least three times daily. The abdominal, gluteal and intrascapular muscles should be faithfully exercised. If the hip and knee joints are acutely involved, adhesive traction may be necessary. When the patient is able to be up, the spine should be protected by a carefully fitted Taylor back brace or removable plaster jacket until it has become completely quiescent. The cervical

spine may need traction with a head sling during the very acute stage. Later, a Thomas collar, made from Bristol board, padded with felt or sponge rubber and carefully fitted to the neck, shoulders and mandibles, gives adequate support. If the spine becomes solidly ankylosed, symptoms disappear, and apparatus may be discarded.

Progressive involvement of the hips presents a problem as yet unsolved. During the early stages, every effort should be directed toward the prevention of flexion deformity, so that walking will not be interfered with unduly, but if the progress of the disease cannot be arrested short of ankylosis of the hips, they should be placed in a position of 30° to 60° flexion so that the patient will be able to sit comfortably. The same general plan should be followed for knee involvement. The restoration of joint function by means of arthroplasty of the hips is very difficult of attainment and should be attempted only by a skilled orthopedic surgeon. The employment of a vitalium metal cup over the femoral head, as described recently by Smith-Petersen,¹⁴ gives far better results than the use of fascia lata. Deep x-ray therapy to the spine and sacroiliac joints is occasionally helpful in the relief of symptoms but does not arrest the progress of the disease:

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It is hoped that this brief review will convince many doubting physicians that good therapy is available for the patient with rheumatoid arthritis, and that if it is carried out religiously and with enthusiasm, it will frequently give very gratifying results.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE MORTEM AND POST MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28381

PRESENTATION OF CASE

A sixty five year old man was admitted to the hospital because of intense abdominal pain.

For more than five years before admission, the patient had suffered with a feeling of fullness and gas after meals. Occasionally, brief attacks of epigastric pain occurred that were not related to food indiscretions and bore no apparent relation to meals. These symptoms were relieved by "cream of tartar." The patient also employed cream of tartar as a laxative, however, the constipation was only of a mild type. He occasionally noticed bright red blood on the outside of his stools, particularly after a "drinking" bout.

Six hours prior to admission, while straining at stool, the patient felt "something explode" with in his abdomen. Extreme nonradiating pain developed about the umbilicus. He did not vomit or move his bowels. He had been well the night before and had had a normal bowel movement on the previous day. He then drank a small amount of water, which was immediately vomited. The pain rapidly increased in severity and became widespread, but was severest in the epigastrium and about the umbilicus. The patient did not suffer with chills or fever. He had never suffered a similar previous attack.

The family and past histories were irrelevant except that the appendix had been removed eight years previously at this hospital.

Physical examination revealed a thin, restless man who was obviously extremely ill. He groaned and complained severely of his pain. Examination of the heart and lungs was negative. The abdomen was extremely rigid, but not distended. The abdominal wall was tender even to light palpation, particularly about and to the right of the umbilicus. No peristaltic sounds were audible. Rectal examination revealed a moderately enlarged prostate and a posterior internal hemorrhoid.

The blood pressure was 130 systolic, 80 diastolic. The temperature was 99°F, the pulse 80, and the respirations 26.

Examination of the blood showed a red cell count of 3,880,000 with a hemoglobin of 70 per

cent, and a white cell count of 20,700. The urine had a specific gravity of 1.015 and was acid in reaction, and the sediment contained 10 to 20 hyaline casts, 1 granular cast and 4 or 5 white blood cells per high power field. A flat plate of the abdomen showed no air under the diaphragm.

The patient was operated on immediately after admission.

DIFFERENTIAL DIAGNOSIS

DR ERNEST M. DALAND: This was an acute abdominal emergency, the patient coming in six hours after the onset of pain. We think immediately of the possibility of a pre-existing gastric lesion, such as an ulcer, but the first paragraph does not give a very clear picture of such a condition. There was no definite relation of his symptoms to meals, and apparently the pain was not relieved by food but was relieved by cream of tartar, which is acid potassium tartrate. I do not know whether that is used in the same way as soda is, and I do not know the significance of relief by cream of tartar.

We are told that this man was thin, restless, extremely ill, groaning and complaining of severe pain. The abdomen was extremely rigid but not distended. The symptoms seem to have been centered around the umbilicus and somewhat on the right side. In this region, we think of abnormalities of the gall bladder, duodenum and pancreas. I think the sudden onset rules out perforation of the gall bladder. The gall bladder does not perforate unless it is gangrenous, and this was a little too rapid for a gall bladder to become gangrenous and rupture. There may have been a diverticulum of the duodenum that had ruptured. The possibility of carcinoma of the stomach must be considered. However, the symptoms went back five years, and there is no evidence that they had particularly changed during the last few months. Perforation of a carcinoma of the stomach is a very rare condition, although it does occur and simulates a perforated ulcer. Mesenteric thrombosis should be considered. The rigidity was quite generalized, although a little more marked on the right. This is a rather rapid history for mesenteric thrombosis, however. The usual story in this condition is a warning sign of mild pain at the time the thrombosis starts,—an interval of a few hours,—and then sudden violent pain due to change in circulation. Acute pancreatitis, I think, can be ruled out on the same basis. This is too rapid an onset to go on to perforation of the pancreatic capsule. Obviously, the patient did have some type of perforation.

I should like to know whether this patient had any sugar in his urine, because diabetic coma can

simulate a perforated gastric ulcer. I once was called to the Emergency Ward to see a patient with an acute abdominal history. The story seemed to be perfectly typical of perforated ulcer. I was told that the patient was in the third room, went down and examined him, put my hand on his belly and said, "This is a typical belly of a ruptured ulcer." Then someone said: "This is the wrong patient. This patient has diabetic coma. Your patient is in the next room." I have never forgotten it.

DR. TRACY B. MALLORY: The qualitative test for sugar was positive; it was not quantitated.

DR. DALAND: I doubt very much if this was diabetic coma. The sudden onset rules it out, but it should be thought of.

My opinion is that this patient had a perforated peptic ulcer, even though the history is not typical. The clinical finding of extreme rigidity in an extremely ill patient to me means perforated peptic ulcer.

DR. MALLORY: I take it then, Dr. Daland, that you believe this patient should have been operated on immediately. Where would you make your incision?

DR. DALAND: I should make a right upper rectus-splitting incision.

DR. MALLORY: That was done on this patient, and a perfectly normal stomach and duodenum were found. With further exploration, pus appeared to well up from the left lower quadrant.

Would you care to speculate on what you might have done at that point?

DR. DALAND: I think I should have made another incision.

CLINICAL DIAGNOSIS

Perforated peptic ulcer.

DR. DALAND'S DIAGNOSIS

Perforated peptic ulcer.

ANATOMICAL DIAGNOSIS

Perforated carcinoma of sigmoid.

PATHOLOGICAL DISCUSSION

DR. MALLORY: A second incision was made in the lower left rectus muscle, and an obvious carcinoma of the sigmoid was found with a perforation through it. The sigmoid was then exteriorized through the abdominal wound. There was, of course, an obvious general peritonitis. The patient survived only a few days.

At the time of autopsy, nothing further was found that would account for any of the symptoms. It was quite clear that the spontaneous per-

foration of the sigmoidal carcinoma was the source of the immediate symptoms.

DR. D. N. SWEENEY, JR.: It is of some interest that after the patient's death his wife admitted that she had given him three enemas, which obviously passed through the perforation and thus aided the rapid generalization of the peritonitis.

CASE 28382

PRESENTATION OF CASE

A forty-year-old secretary entered the hospital complaining of fatigue and shortness of breath.

The patient felt perfectly well until she was nine years of age, when, during the course of a summer, without symptoms and without pain, she developed a crooked back. For several years thereafter, she performed daily orthopedic exercises without apparent benefit, and the deformity seemed to progress. Various overcorrecting braces were applied, but these were very uncomfortable and gave no relief. For many years, the patient had worn a supporting brace during the day; this was comfortable and relieved fatigue.

Ever since the deformity appeared, that is, for the previous thirty years, the patient had suffered from dyspnea and fatigue on exertion, which tended to progress very slowly. Two years before admission, during a period of unusual emotional and physical strain, the patient became very nervous and suffered from extreme fatigue and dyspnea on the slightest exertion, the whole culminating in an almost complete breakdown one year before entry. She took a long holiday, and very gradually her strength returned, so that six months before admission she resumed secretarial work. Soon, however, weakness and fatigue reappeared and reached a point where the hands trembled during work and she had to rest several times during the short walk home, sometimes fell asleep at the evening meal, and seemed dazed on being awakened.

The patient had occasionally noticed palpitation but no dizziness, fainting, edema, cyanosis, chills, fever, cough or loss of weight. Although shortness of breath appeared on the slightest exertion, it was not present during rest, and she was most comfortable when lying perfectly flat on her back.

The family history was irrelevant. The patient had suffered from the usual childhood diseases; there was no history of poliomyelitis, tuberculosis or rheumatic fever. An ovarian cyst had been removed twelve years before admission, and the patient stated that she had had a "heart murmur" for many years.

On examination, the patient was frail, with rapid, shallow breathing and deep cyanosis of the lips and fingers. Distended veins were present in the right neck, but not on the left, and no pulsation was visible. In the spine, there was an extreme dorsal scoliosis, with the convexity to the right, a moderate lower dorsal lordosis and an upper dorsal kyphosis. The sternum was just to the right of the midline, and a slight depression was present in the right chest anteriorly and the left chest posteriorly. Chest expansion was poor, but the lungs were clear.

Cardiac dullness extended into the entire left axilla and about 4 cm. to the right of the mid-sternal line. An impulse was felt in the left chest posteriorly, the rate varied between 70 and 103, and there were occasional extrasystoles. A loud harsh systolic murmur was heard throughout the left axilla and to a lesser extent in the aortic area. The pulmonic second sound was loud, and both sounds were rasping in this area. The abdomen was tense, with percussion dullness in the right upper quadrant to the umbilicus and in the left upper quadrant to three fingers below the costal margin; no organs could be felt. There was no peripheral edema. Examination of the nervous system was negative.

The blood pressure was 125 systolic, 80 diastolic. The temperature was 99.5°F., the pulse 90, and the respirations 20 to 30.

The urine showed a ++ test for albumin. The blood revealed a red-cell count of 5,900,000 with a hemoglobin of 14.5 gm. (photoelectric-cell technique), and a white-cell count of 6700.

An electrocardiogram showed normal rhythm, with sinus arrhythmia in Lead 2 and a PR interval of 0.14 second. There were low voltage in Lead I, a low R₄, an elevated ST₄ and an inverted T₄. There was a tendency to right-axis deviation.

The patient was digitalized rapidly and that night became irrational, restless, frightened and suddenly more cyanotic, with marked venous engorgement. Tourniquets were applied to the extremities, an oxygen tent used, and later, the orthopedic brace was fitted on. The next day, the patient's pulse was stronger, the color better and the respirations deeper, although she had lapsed into coma with deep cyanosis and paroxysms of muscle twitching in her arms and legs; a 500-cc. venesection had no apparent effect. On the third hospital day, there was some improvement, and the patient became coherent; on the following day, however, she again became comatose. An electrocardiogram showed no essential change since the previous tracing. Death occurred on the fifth

hospital day. At no time were there abnormal neurologic signs or peripheral edema.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT E. GLENDY: This history, in brief, is that of a middle-aged woman with a severe dorsal spinal deformity of thirty years' duration, long-standing progressive dyspnea and fatigue on exertion, manifest cardiac enlargement and, finally, an unusual train of symptoms, including extreme dyspnea, cyanosis, unilateral venous engorgement in the neck, accentuation of the pulmonic second sound, poor chest expansion but clear lungs, some ascites but no peripheral edema, and a normal blood pressure. It was the progression of these pulmonary and cardiovascular signs and symptoms that resulted in her death. The problem therefore resolves itself into one of establishing the underlying factors that would produce such a picture.

At the age of nine, the patient developed a crooked back, which was painless and without symptoms except for the dyspnea and fatigue that attended the deformity almost from the outset. The chief curvature of the spine is described as one of extreme dorsal scoliosis. Lateral curvature of the spine may be the result of muscular unbalance, congenital defects of the vertebrae, irregular growth of the vertebral bodies, as in rickets, and destructive lesions causing lateral collapse of the vertebra. Just which of these factors was responsible in this case is not clear. The age at onset rules out a congenital defect. There was no paralysis or other neurologic abnormality that would point to such conditions as spastic paralysis and syringomyelia. No mention is made of empyema or thoracic surgery, which sometimes produce thoracic deformities. The irrelevant past and family histories, the absence of pain and the type of deformity are against the possibility of a tuberculous spine. This leaves poliomyelitis or some disturbance in the growth of the vertebral bodies as the remaining possibilities. There is no history of the former, but either one could produce such a deformity of the spine, and for the purposes of this discussion, no further conjecture seems necessary. The deformity, running true to form, increased rapidly during puberty, in spite of orthopedic treatment, and because of secondary changes in the thorax undoubtedly caused cramping and distortion of the lungs, heart and great vessels.

Before developing this idea further, however, let us consider the history and findings for other cardiovascular etiologic relations. There was no

history of rheumatic infection, and yet the patient had a harsh systolic murmur, heard best in the left axilla, which could have been due to valvular heart disease (mitral regurgitation). The strongest argument against this is the fact that she had symptoms pointing to a poor cardiac reserve for many years—in fact, from the very time that the spinal deformity appeared. This is certainly not the usual history of mitral regurgitation, which, as a rule, acts as a benign, well-compensated lesion for long periods before signs of myocardial insufficiency appear. My guess is that no organic cause for this murmur will be demonstrated at autopsy other than dilatation of the heart. The fact that the patient was perfectly well during her early childhood is very much against any significant congenital heart lesion. From the evidence presented, hypertension and coronary disease deserve no serious consideration as underlying factors, nor does syphilis. Therefore, in the absence of any of the usual etiologic factors in heart disease, I am forced to the conclusion that the distortion of the thoracic viscera secondary to the spinal deformity was the underlying cause of the trouble. Occurring so early in life, the thoracic deformity must certainly have impaired the development of the lungs. This would account for the habitual dyspnea for so many years.

The entire picture seems to conform completely with the syndrome described by Chapman, Dill and Graybiel,* which occurs in persons afflicted with severe deformities of the chest and spine and has been called by them "pulmonocardiac failure." The most striking feature of their studies on a group of patients with scoliosis from the Orthopedic Department of this hospital was the absolute and relative reduction in lung volume. Additional evidence that the chief effect of this syndrome is on the lungs was found in the clinical facts that respiratory depressants, pulmonary infection, cramped position or anything that further reduces pulmonary function may lead to attacks that resemble sudden heart failure. Their account of the symptoms and signs of this condition include habitual dyspnea, persistently rapid heart rate, accentuation of the pulmonic second sound, right-sided cardiac enlargement (by fluoroscopy), occasional right-axis deviation in the electrocardiogram and, as the disease progresses, attacks of paroxysmal dyspnea, great weakness and fainting, which mark the onset of pulmonocardiac failure. Once these severe symptoms appear, the interval before death is usually short.

*Chapman, E. M., Dill, D. B., and Graybiel, A. The decrease in functional capacity of the lungs and heart resulting from deformities of the chest: pulmonocardiac failure. *Medicine* 18:167-202, 1939.

Without enumerating each sign and symptom again, I believe that this patient followed the clinical pattern outlined above quite closely. The detection of cardiac enlargement in the presence of severe thoracic deformity is difficult, but, judging from the area of cardiac dullness described in this case, I should predict that post-mortem examination will show enlargement of the heart, particularly the right ventricle. In view of the age at the onset of the chest deformity, it is likely that the lungs were poorly developed and entirely inadequate for adult development. This decrease in actual lung substance may also be attended by areas of atelectasis or emphysema, or both. One might anticipate an infection in the lungs that acted as an additional precipitating factor to the cardiac failure, but nothing is recorded in the history to support this idea except slight fever (99.5°F.) on admission. The presence of unilateral (right) venous engorgement in the neck and ascites suggests that the distortion of the heart and great vessels may have been so great as to interfere with the drainage of both the superior and inferior vena cavae.

CLINICAL DIAGNOSES

Pulmonocardiac failure.
Scoliosis.

DR. GLENDY'S DIAGNOSES

Pulmonocardiac failure, secondary to cramping and distortion of thoracic viscera from severe dorsal scoliosis of obscure etiology (poliomyelitis or growth disturbance in vertebrae).
Cardiac hypertrophy, predominantly right ventricular.
Maldevelopment of lungs.

ANATOMICAL DIAGNOSES

Kyphoscoliosis, right dorsal, extreme.
Degeneration of anterior horn cells of spinal cord.
Cor pulmonale, slight.
Pulmonary hypoplasia.
Acute passive congestion.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This case is a very characteristic example, as Dr. Glendy has pointed out, of so-called "pulmonocardiac failure" based on spinal deformity. This syndrome, which has been well recognized in Europe for many years, received very little attention in this country until the studies of Chapman, Dill and Graybiel. These

studies were important not only in calling attention to this by no means rare condition but also in demonstrating that the very low reserve of these patients is due to a marked reduction in all components of the vital capacity. Although the symptoms usually suggest right-sided heart failure, the degree of cardiac abnormality is usually not very great.

In this patient, the right auricle was greatly dilated, and the right ventricle a little dilated and also slightly but definitely hypertrophied. The left side of the heart, the valves and the coronary arteries were entirely normal. The viscera were acutely congested, but there was no evidence of severe and long-standing passive congestion, such as one might expect in the cor pulmonale of Ayerza's disease. The lungs were of normal

weight but small volume. The right lower lobe, in particular, was a mere shell, 5 to 10 mm. in thickness. All lobes, however, were aerated, and there were no foci of either atelectasis or emphysema.

The cause of the scoliosis remains in doubt. There was no disease of the vertebrae, either congenital or acquired, but the spinal cord showed extensive loss of ganglion cells. I should have accepted this as evidence of old poliomyelitis, but Dr. Charles S. Kubik believed that the findings were not sufficiently typical and that some other neurologic disorder must be assumed. He refused, however, to commit himself regarding what this might be. Unfortunately, we did not have permission to examine the entire central nervous system.

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"BUSINESS AS USUAL"

THE proprietor of one of Boston's most respectable bars (although associated in no official way with the legal profession), a spectator of man's progress onward and downward, has been credited with the observation that our drinking habits have changed. Since the immensity of our war problem has impressed itself on us, we have turned, paradoxically enough, to sober drinking. We sip our liquor seriously, even sadly. As our spirits go down, our spirits go down: this, at least, has been the judgment of one with every opportunity for an analysis of the situation.

It is true that the task to which we have set ourselves has touched the lives and is affecting the

destinies of everyone in our country, to put it provincially. Many have dedicated their lives entirely to it, and not a few have already given their lives for it; many have as yet had little of the burden to bear, although the majority will be ready when each one's way is clearly shown. Our thoughts are constantly colored by the changed atmosphere in which we live, the altered tenor of our ways, the anxiety of the days through which we are passing and the uncertainty of the relentless future, when that presents its bill.

We have been told repeatedly, by the authorities to whom we have delegated the regulation of our affairs, that we must turn completely from our sinful ways, "or else . . ." that we must give ourselves entirely to the war effort, that frivolity is finished, profit is outlawed and "business as usual" is through. All of which is good, sound, wholesome advice, provided there does not appear so much scribbling on the wall that he who runs will have to stop and lose the race while he reads it.

Our leaders, of course, are right, and they are doing a very serious and important job in a very serious and important manner. To a certain degree, — and we must resign ourselves to our American tendency to overdo everything, — we must be treated like children. We must accept not only direction but chiding and nagging, for that is the parent's anxious way.

We must also remember, however, that too great an emotional concentration on a heroic task may have its paralyzing effect as well. There are still other things to do besides concentrating on a supreme effort and fumbling with a radio dial. The tension of the concentrated effort has its natural reaction in a temptation to dispersal of our energies in all other directions. What is left of our maligned "business as usual" may seem so trite that a determination equivalent to heroism is required to get at it and get it done, but the stabilizing value of what can decently remain of it must not be neglected even in the glare that comes from the forge of Vulcan. The fundamental sanity of also keeping our home fires burning, despite domestic fuel reduction, should not be lost sight of entirely.

CONSTITUTIONAL INADEQUACY

CONSTITUTIONAL inadequacy may become a new diagnosis to be added to the already overcrowded nomenclature. Alvarez* has recently called attention to the many patients who are "always weak and tired and full of pains and always getting sick in one way or another." They have numerous operations and repeated treatments for various organs of the body, and still do not get well. Several different types of this syndrome are outlined. Reference is made to asthenic persons who cannot stand much work, excitement or loss of rest, to the women who are troubled with their pelvic organs and, perhaps, with their glands of internal secretion, to those who have a poor resistance to infections of all kinds and a poor ability to recover from them, to those who become senile early in life, to persons whose symptoms are mainly those of an irritable colon, and to those who complain of "nervousness," who are worrying and who are continually running to a physician for this or that minor ailment. Of course, there are many frail, sickly looking persons who have sufficient energy to perform their daily work, or perhaps to perform outstanding feats in the face of all sorts of illness and discouragement, they are not inadequate in any sense of the word.

It is a universal desire to leave no stone unturned in the search for health by all the new developments of modern medicine. This inadequacy, however, is to be suspected whenever disabilities of various kinds and feelings of great fatigue have been present for years without bringing disaster, whenever the severity of the symptoms is out of all proportion to the disturbances found on examination and whenever the aches and pains are scattered too widely to be explained on the basis of any one lesion. It seems likely that the fundamental cause is in the nervous system, but whether a separate label beyond those already used is necessary for this inadequate group is a moot point.

In the past, numerous miracles have been wrought by the removal of foci of infections and by the use of hormones, vitamins and other newly discovered therapeutic agents, but many failures are recorded and a large amount of unnecessary treatment has been given. This diagnosis, therefore, must be used with discrimination. It is imperative that the physician, especially in borderline cases, make a careful estimate whether the findings in a given patient warrant operative interference or a long course of treatment and whether there is a reasonable probability of bringing about real health. A full knowledge of this syndrome and its use in suitable cases will undoubtedly lead to the avoidance of unnecessary therapy. But, if the diagnosis is employed, physicians must adopt a technic of explaining the situation to their patients in such a way that the latter will accept [the] verdict of constitutional inadequacy without annoyance or rebellion and will decide to mend their bad psychic ways, to hoard their energies and to live within their limited means of strength.

MEDICAL EPONYM

RIGGS'S DISEASE

A paper read before the American Academy of Dental Surgery in New York on October 20, 1875, by John W. Riggs (1810-1885), M.D., F.A.A., D.S., of Hartford, Connecticut, entitled "Suppurative Inflammation of the Gums and Absorption of the Gums and Alveola [*sic*] Process," has served to attach his name to the condition of pyorrhea. This appeared in the *Pennsylvania Journal of Dental Science* (3:99-104, 1876). A portion of the text follows:

This disease is called by many the disease of old age but at the present day we find the middle aged, and even the young, affected by it. One by one the teeth become loose from loss of bony support and are plucked out as an intolerable annoyance. If the inflammatory action be great and involve most or all the gum embracing the teeth pus tinged with blood exudes from around the necks of the teeth on the slightest pressure of the lips or tongue, or in mastication. The oral secretions become vitiated, present a viscid or saucy character, very abundant in quantity during the day, but much more so in the recumbent position of sleep. If the patient reposes on his side these exudations flow out of the corner of the mouth

*Alvarez, W. C. Constitutional inadequacy. *J. A. M. A.* 119: 80-83, 1942.

over the pillow and present in the morning a dried, yellow discoloration, often tinged with blood and covering a space as large as one's hand. If the patient reclines on his back the diseased mass flows back into the fauces and is unconsciously swallowed, then to work a greater mischief. . . . None but the most vigorous constitutions can withstand this type of disease.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

STATED MEETING OF THE COUNCIL

A stated meeting of the Council of the Massachusetts Medical Society will be held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, October 7, 1942, at 10:30 a.m.

Business:

1. Call to order at 10:30 a.m.
2. Presentation of record of meeting held May 25 and 26, 1942. (Published in the *New England Journal of Medicine*, issue of June 25, 1942.)
3. Reports of standing and special committees.
4. Appointment of an auditing committee.
5. Fill any vacancies in the offices of the Society.
6. Such other business as may lawfully come before this meeting.

MICHAEL A. TIGHE, M.D., *Secretary*

IMPORTANT REPORTS TO BE CONSIDERED BY THE COUNCIL

SURVEY OF STATE-AIDED CANCER CLINICS

At your request, I have made a survey of the state-aided cancer clinics and beg to submit the following report:

I have visited each clinic, with one exception, during the spring and summer and have also attended most of them previously. Of the one clinic not visited recently, I have some knowledge and have received reports from men who have conducted their teaching clinics.

It is difficult to determine the value of the cancer clinics alone, for they represent only part of the state cancer-control program. There are twenty-three consultation clinics, including those connected with the state cancer hospitals at Pondville and Westfield. The two hospital clinics are excellent in every way and will not be considered.

In 1941, 1782 new cases of cancer were seen at the clinics. This is estimated to be 8 per cent of the patients with cancer living in Massachusetts in a year. At first glance, this seems a small percentage, but it is probable that in most cases the remaining patients are receiving adequate care from their own physicians, are seen in private consultation, or have consulted the tumor clinics maintained by many of the larger hospitals. Most of the patients seen in the clinics are impecunious, although in certain localities, notably Beverly, Lowell and Lynn, it is not unusual for physicians to refer their well-to-do patients for consultation.

The statistical data of the clinics for the year 1941 are shown in Table 1; 5117 new patients consulted the clinics, of whom 1782, or 35 per cent, had cancer. The total attendance was 26,118.

Organization

The consultation cancer clinic is generally accepted as being one of the best methods of controlling the disease. Clinics similar to those in Massachusetts have been set up in the rest of the country and in general follow the rules laid down for cancer clinics by the American College of Surgeons. Group consultation is advocated, all patients being seen by a clinician, a radiologist and a pathologist, but it is impossible to conform to this requirement in certain communities. The best organized clinics consist of a permanent committee, one of whom is present at each clinic, supplemented by a rotating staff composed of the surgeons connected with the local hospital. This setup obtains in only a few clinics, however, but should be more generally adopted. Each clinic has attached to it a full-time or part-time social worker and a secretary.

Functions

The function of the clinics is fivefold: to furnish consultation; to furnish treatment at the state cancer hospitals when it is indicated and requested; to follow up treated cases through the social-service worker, to determine the results of treatment, and to advise further procedures if necessary; to educate the public in regard to cancer through the knowledge that such a clinic functions in their community; and to educate the practitioners in the community in the early diagnosis and modern treatment of cancer through consultations and teaching clinics.

Finances

The clinics are maintained at a considerable expense. The budget for the year 1942 is \$28,000, which is a cut from previous years. About half is designated for salaries for social workers (\$14,260 in 1941). The appropriations are placed in the hands of the committee in charge of the individual clinic, to be expended as in their judgment seems best. The other items of expense vary greatly in the different clinics for no obvious reason. One clinic has a charge of \$409.70 for "traveling expenses," whereas only two others have a charge under this heading, and both are under \$10. I question the need of this expenditure. The Boston Dispensary clinic has a charge of \$1125.20 for "diagnostic procedures" on 573 patients, whereas charges under the same heading in Lynn are \$41.60 for 560 patients. The Lynn clinic is as efficient as any in the State. This suggests on the one hand that the hospital, or patient, has assumed some of the expense of these procedures and, on the other, that the facilities for free diagnosis of patients with suspected cancer may be abused. The Beverly clinic is maintained at a cost of \$0.67 a patient visit, whereas the cost per visit in Pittsfield is \$6.61. Undoubtedly, economies could be practiced in many of the clinics, but this is the responsibility of the committee of physicians in charge, for the Department of Public Health has chosen to work through the medical profession. It may be said that if only 1 life in 8 of the 1782 new patients with cancer disease consulting the clinics in a year is saved by this consultation, a life is worth \$125 in round figures.

The expenses incurred by the clinics for 1941 are given in Table 2.

Teaching Clinics

Out-of-town physicians are invited to hold clinics and give a talk on some special subject two or three times during the year at many of the clinics. Notices of these talks are sent to the physicians in the neighborhood.

These teaching clinics are usually very well attended and, I believe, have an educational value.

SUMMARY OF CLINICS

Beverly. A well-organized and well-run clinic. The figures of attendance suggest a falling off in the number of cases seen, but I do not believe they give an accurate idea of the work. There are facilities for diagnosis and

nosis and all forms of treatment. One hundred and fifty new patients were seen in 1941, of whom 76 had cancer. This is 40 per cent less than the number of cases seen in 1940. Two teaching clinics were held in 1941. Unit cost per visit is \$1.98. The budget is \$3000. It is necessary to continue this clinic.

Boston Dispensary. This is a large, active, well-run clinic. There has been a slight falling off in the number

TABLE 1 *Massachusetts State Aided Cancer Clinics, 1941*

CLINIC	TOTAL	ATTENDANCE*		NEW CANCER PATIENTS	PERCENTAGE OF CANCER AMONG NEW PATIENTS	NO. OF TEACHING CLINICS	ATTENDANCE OF PHYSICIANS AT TEACHING CLINICS	SOCIAL SERVICE CONTACTS
		NEW PATIENTS	OLD PATIENTS					
Beth Israel Hospital	1615	161	1454	80	49.7	0	0	132
Beverly	350	69	281	18	26.1	0	0	768
Boston Dispensary	2467	429	2038	132	30.7	1	103	1666
Brookton	267	137	125	64	46.7	3	68	1031
Fall River	686	142	544	54	38.0	4	143	485
Fitchburg	240	44	196	15	34.1	4	26	746
Gardner	176	50	6	17	34.0	5	71	422
Glooucester	96	33	63	12	36.3	3	41	285
Greenfield	51	11	40	5	45.4	1	15	72
Hyannis	104	24	80	13	54.2	2	29	261
Lawrence	219	129	90	57	44.1	5	91	1217
Lowell	345	156	189	41	26.3	0	0	1017
Lynn	107	249	828	111	44.2	0	0	2752
New Bedford	523	166	357	69	41.6	0	0	1685
Newburyport	76	25	51	6	24.0	4	33	217
North Adams	40	7	33	4	57.2	0	0	181
Pittsfield	49	10	39	2	30.0	0	0	157
Pondville Hospital	9153	1503	7650	515	34.2	0	0	—
Quincy	71	17	54	3	17.7	0	0	179
Salem	599	139	460	50	36.0	4	154	1154
Springfield	282	90	192	19	21.1	0	0	1583
Westfield Sanatorium	6534	1229	5305	428	34.8	1	37	—
Worcester	1153	297	856	67	22.5	1	37	2148
Totals	26118	5117	21001	1782	34.8	39	898	—

*Some patients went to more than one clinic.

all forms of treatment. Sixty-nine new patients were seen in 1941, of whom 18 had cancer. Unit cost per visit is \$0.67 (the smallest of any clinic). The budget is \$250. This clinic should be continued.

Beth Israel Hospital, Boston. This is a large clinic conducted by a very competent radiologist, a pathologist be

liever and all forms of treatment. Of 429 new patients referred to the clinic in 1941, 132 had cancer. There are facilities for diagnosis only—none for surgical or high voltage x-ray treatment. It is difficult to separate the patients seeking advice in the state-aided clinic from those referred from the general outpatient clinic. There

TABLE 2 *Massachusetts Cancer Clinics—Total Expenditures in 1941*

NAME OF CLINIC	SOCIAL WORKER'S SALARY	SOCIAL WORKER'S TRAVEL	CLERICAL HELP	DIAGNOSTIC PROCEDURES	TEACHING CLINICS	TRAVEL OF COMMITTEE	OFFICE SUPPLIES	TRANSPORTATION OF PATIENTS
Beth Israel Hospital	\$1699.92	\$14.65	\$ 82.50	\$769.84			\$50.00	\$18.00
Beverly	96.00	43.93	160.50	62.50			45.15	
Boston Dispensary	1560.00	169.33	1124.20	1107.00	\$431.98		27.50	52.10
Brookton	800.00	500.00	469.00	41.00	114.30	\$409.70	106.32	50.00
Cape Cod	33.00	92.69	75.75	6.00	85.00		60.65	
Fall River	124.98	11.05	259.02	47.50	248.35		180.48	14.20
Fitchburg	65.55	36.91	265.17	50.00	88.68		13.00	
Gardner	100.90	54.33	200.00	125.00	194.85	20	47.80	5.00
Glooucester	53.00	29.52	100.85	25.50	139.35		58.47	
Greenfield	143.75	29.20	85.00	9.75	50.00		44.80	
Lawrence	869.00	153.87	282.80	40.00	139.39		132.21	
Lowell	1066.26	45.05	360.00	9.00			28.39	3.10
Lynn	1250.00	135.50	1137.89	41.50	25.00		37.45	294.75
New Bedford	1030.16	14.00	5.00	168.00			111.06	60.30
Newburyport	23.50	22.50	314.07	60.00	83.85	4.78	20.70	
North Adams	160.00	34.68	88.00	25.00			6.06	75.00
Pittsfield	150.00	61.13	264.00	35.00			11.07	
Quincy	42.73		18.68	52.25			6.62	
Salem	10.20	44.02	425.06	166.75	164.97		239.64	
Springfield	1800.00	146.00	144.00	25.00	15.80		78.16	
Worcester	1800.00	194.62	548.00				173.00	90.42
Totals	\$14260.25	\$1994.02	\$ 674.49	\$2867.59	\$1 81.52	\$471.58	\$14 8.03	\$663.62

ing available at all times. The hospital has only fifty to sixty ward beds, the remainder of the beds being reserved for private patients. There are facilities for diag-

is a charge of \$1125.20 for "diagnostic procedures" for 575 patients that might be compared with Lynn which has a charge under this heading of \$41.60 for 560 pa-

tients. Unit cost is \$1.62. The budget is \$3500. This clinic should be continued.

Brockton. This is a relatively active clinic that does not function in a very satisfactory manner, probably because of local conditions. Little interest appears to be taken in the clinic by the practitioners in the city. It is held at the Brockton Hospital, and certain of the physicians in charge of the clinic are not on the staff of that hospital and their authority is therefore limited. There are facilities for diagnosis and surgical treatment only. Patients requiring radiation treatment or special investigation are referred to Pondville Hospital. One hundred and thirty-five new patients were seen in 1941, of whom 60 had cancer. This is about half the number of cases of cancer seen in 1935. There were four teaching clinics held during this year. Considering the population of the city, the clinic should be larger. Unit cost is \$4.33. The budget is \$2000. Brockton is relatively close to the Pondville Hospital, and unless more interest is shown by the medical profession of Brockton, the advisability of discontinuing the clinic should be considered.

Fall River. This is an active clinic under the charge of a committee one member of which is usually present on each clinic day. On the day of my visit, five visiting physicians were present. There are facilities for surgical consultation and radiologic and surgical treatment. Besides the general clinic, there is a special gynecologic clinic. Four teaching clinics were held in 1941, with a large attendance. One hundred and forty-two new patients were seen in 1941, of whom 54 had cancer. On the day of my visit, 19 patients were examined. This is a well-managed, active clinic, considering the fact that there are three hospitals in Fall River. Unit cost per visit is \$1.13. The budget is \$800. This clinic should be continued.

Fitchburg. This is a relatively active clinic conducted by a permanent staff; a surgeon and a radiologist are usually present, but no pathologist is attached to the hospital. There are facilities for consultation and radiologic treatment. The clinic is somewhat hampered, for many of the younger men have entered the service. On the day of my visit, there were 10 patients. In 1941, 44 new patients were examined at the clinic, of whom 15 had cancer. Three teaching clinics were held in 1941. Unit cost per visit is \$1.45. The budget is \$500. This clinic should be continued.

Gardner. This is a well-organized and well-run clinic. All the practitioners in the vicinity seem interested. Dr. Pierce, former director, is now in service, but his place has been taken by Dr. Thompson. Consultation and facilities for surgical and radiation treatment are offered. Fifty new patients were seen in 1941, of whom 17 had cancer. Five teaching clinics were held during that year. Unit cost per visit is \$2.95. The budget is \$600. The clinic should be continued.

Gloucester. This is a well-organized clinic administered by a permanent committee and a rotating staff. It offers consultation and facilities for surgical treatment only. No pathologist or radiologist is available. The clinic is small, but the local men apparently take considerable interest in it. Forty-four new patients were seen in 1941, of whom 6 had cancer. Three teaching clinics were held during that year. Unit cost per visit is \$2.33. The budget is \$200. The clinic should be continued.

Greenfield. This clinic was discontinued in 1933, was reopened in 1935, and was again discontinued in 1941. A

committee of the Hampden County Medical Society then drew up recommendations regarding the conduct of the clinic, and it was reopened in 1942. The chairman of the committee, I understand, has attended only one clinic during the year. On the day of my visit, no member of the committee was present. The city apparently wants the clinic, but little interest is taken in it. There are facilities for consultation and surgical treatment only. Thirty-three new patients were seen in 1941, of whom 12 had cancer. Unit cost per visit is \$4.50. The budget is \$600. If the physicians of the locality are not willing to support it in a more active manner, this clinic should be discontinued.

Hyannis. This clinic is practically administered by one man and not by a committee. The physicians in the locality are not co-operative. How much of this is due to the manner in which the clinic is conducted, it is impossible to say. The clinic should be managed by a committee, but it is difficult to find men in this community particularly interested in or having a knowledge of cancer. The budget is large, particularly certain items in the expense account (Table 2). Twenty-four new patients were seen in 1941, of whom 13 had cancer. Unit cost per visit is \$4.28. The budget is \$700. Several teaching clinics were held, which were well attended. This clinic does not function in a satisfactory manner, and I should advise discontinuance except for the fact of its geographical situation, for it serves the entire Cape Cod area. It might well be reorganized.

Lowell. This is an excellent and well-organized, well-run clinic in charge of a permanent committee, one of whom is always present, assisted by a rotating staff. Much interest is shown by the physicians and patients. Consultation and treatment facilities, for both surgery and radiation, are available. One hundred and fifty-six new patients were seen in 1941, of whom 41 had cancer. Unit cost per visit is \$1.74. The budget is \$1500. This clinic should be continued.

Lawrence. This is an active clinic in which much interest is shown by the local profession. A pathologist and a radiologist are available if not present at each clinic, as well as a clinician. There are facilities for consultation as well as for radiation and surgical treatment. Five teaching clinics were held in 1941. One hundred and twenty-nine new patients were seen in 1941, of whom 50 had cancer. Unit cost per visit is \$3.22. The budget is \$1700. The clinic should be encouraged.

Lynn. This is an active, well-run general clinic as well as a special genitourinary and gynecologic clinic. It has the support of the local physicians, many of whom refer their well-to-do patients for consultation. There are facilities for consultation as well as for surgical and x-ray treatment. Two hundred and forty-nine new patients were seen in 1941, of whom 122 had cancer. Unit cost per visit is \$2.33. The budget is \$3000. The clinic should be continued.

New Bedford. This is a good setup and, on the whole, a well-run clinic. A full-time radiologist and surgeon are in attendance. There is consultation, surgical and radiation service. The patients are almost entirely from New Bedford—rarely from the surrounding towns. A surgeon and a radiologist are present at every clinic. Many of the younger men who formerly attended the clinics are now in service. One hundred and sixty-six new patients were seen in 1941, of whom 69 had cancer. Unit cost

per visit is \$2.37 The budget is \$7000 This clinic should be continued

Newburyport This clinic is not satisfactory The professional standards in Newburyport are as high as those in any other community, but there is no surgeon or radiologist in the city or any physician with special training in the treatment of cancer Little interest is taken in the clinic by the local men Cancer cases requiring consultation are sent either to Boston or the Pondville Hospital, or private consultation is obtained Twenty five new patients were seen in 1941, of whom 6 had cancer Unit cost per visit is \$3.16 The budget is \$300 I suggest that this clinic be discontinued

North Adams This is a small clinic in a relatively small community, but the local medical profession takes considerable interest in it and are attempting to build it up Consultation and facilities for surgical treatment only are offered Patients requiring special examinations or radiation treatment are referred to the Westfield Sanatorium Seven new patients were seen in 1941, of whom 4 had cancer Unit cost per visit is \$4.78 The budget is \$400 I believe this clinic should be encouraged and supported

Pittsfield This clinic is unsatisfactory It is in charge of a committee but practically administered by one man who takes considerable interest in it Although Pittsfield is geographically the center of Berkshire County the clinic is not patronized by the physicians in the district, who generally refer cases to either Westfield or Albany Of 42 cancer patients from Berkshire County seen at the state aided clinics in 1941, only 2 were seen first in this clinic There were no patients in the clinic the day of my visit One teaching clinic was held in 1941 There are facilities for consultation and surgical treatment only Ten new patients were seen in 1941, of whom 2 had cancer Unit cost per visit is \$6.61 (the highest of any clinic) The budget is \$300 I suggest that this clinic be discontinued or entirely reorganized The Department of Public Health is investigating the situation

Pondville This is an excellently run and administered general hospital, with an outpatient clinic for the diagnosis and treatment of cancer The clinic and hospital offer all forms of treatment The hospital is handicapped at present by lack of nurses The staff is permanent, and special clinics are held One thousand five hundred and three new patients were seen in the outpatient department in 1941, 515 of whom had cancer There were 9153 outpatient visits The clinic and hospital should be supported and encouraged

Quincy This is a small clinic in which little interest is taken by local men, with the exception of the pathologist Patients on whom consultation is desired are usually referred directly to Boston, and the clinic is not patronized by the surrounding towns The staff is rotating, but only one man was present the day of my visit Eighteen new patients were seen in 1941, of whom 3 had cancer Unit cost per visit is \$1.08 The budget is \$75 I do not believe this clinic will ever increase on account of its proximity to Boston I suggest that it be discontinued

Salem This is an active, well run clinic Consultation services are offered, as well as radiologic and surgical treatment The committee in charge is active and several of the members are present at each clinic Many well-to-do patients are referred to it for consultation by local physicians Four teaching clinics were given in 1941 with an average attendance of 50 Unit cost per

visit is \$3.04 The budget is \$2100 One hundred and thirty nine new patients were seen in 1941, of whom 53 had cancer The clinic should be continued

Springfield This clinic is held in the Springfield Hospital but is served by a rotating staff from the hospital and the other two large hospitals in the city It does not give group-consultation service The chairman of the clinic was not in attendance on the day of my visit but was reached by telephone Many Springfield patients are referred directly to the Westfield Sanatorium Fifty five new patients were examined in 1941, of whom 9 had cancer Only 12 per cent of the cancer cases from Springfield are first seen at this clinic On the day of my visit, 4 patients were present, all follow up cases Unit cost per visit is \$1.25 The budget is \$2000 Considering the proximity of Springfield to Westfield (seven miles) and the lack of local interest, as well as for financial reasons I believe it would be well to discontinue this clinic and have all patients referred to the Westfield Sanatorium

Westfield Sanatorium This is a well run fifty bed cancer hospital equipped to care for and treat any form of cancer and having a large outpatient clinic as well All consultations are held in the general clinic on Wednesday, and patients are referred to the special clinics if necessary The staff is rotating, with a permanent surgeon in charge The clinic and hospital serve the western half of the State, and cases from the Pittsfield and North Adams districts are often referred here for consultation rather than to the local clinics For example, in 1941, of the 22 cases of cancer from the North Adams district, 18 were first seen at this clinic One thousand one hundred and ninety seven new patients were seen in 1941, of whom 564 had cancer The clinic and hospital should be continued

Worcester This clinic is held at the Memorial Hospital, the visiting men are in part from that hospital and in part from the other two large hospitals in the city This is apparently the condition that exists in many of the larger communities supporting more than one hospital The clinic interlocks with the follow up cancer clinic of the Memorial Hospital All forms of treatment are available Much interest is taken by several of the hospital staff and the clinic committee, and some research work is being done at the hospital One teaching clinic was held in 1941 Of 297 new patients seen in 1941, 67 had cancer Unit cost per visit is \$1.67 The budget is \$2700 This clinic should be continued

REMARKS AND CONCLUSIONS

The clinics must be considered a part of the cancer control campaign inaugurated by the Department of Public Health It is very difficult to evaluate the results of the work, but investigations are now being carried on in an attempt to determine what has been accomplished It may be said, however, that the mortality from cancer in the State rose steadily until 1935 but has remained stationary since that year, whereas deaths among women have shown a slight decrease This is not true in the remainder of the country, although the figures for New York State at the present time indicate a similar drop

As I see it, the conception of the consultation cancer clinics and the setup inaugurated by the Department of Public Health are excellent The clinics are for consultation only, and patients requiring treatment are referred to one of the two state hospitals Many patients, however, prefer to have the therapeutic procedure advised carried out at local hospitals if this is possible The success or

failure of the clinic depends entirely on the medical profession of the locality in which it is situated. It also depends on: the chairman of the committee, his energy and organizing and professional ability, and the confidence reposed in him by the physicians in the community; the co-operation of the practitioners in the district—unfortunately jealousies exist in certain communities; the interest of the local physicians; and the antagonism to "state medicine" felt by certain men, who, however, are willing to use the clinics for their impecunious patients.

The best setup of the clinics consists of a committee one of whom is present at every clinic assisted by a rotating visiting staff including a radiologist. This organization is impossible in certain centers, and the same standards cannot be demanded of a clinic situated in a small community, such as North Adams, as should prevail, for example, in Boston or Worcester. The activities of the cancer-control program and the clinics will probably be curtailed on account of the war. Many of the younger active men are in service, and the transportation of patients to the clinics is becoming increasingly difficult.

So far as finances are concerned, economies could probably be practiced in certain of the clinics, but this is the province of the local committees.

The teaching clinics are very well attended on the whole, and the advisability of holding them more frequently should be considered.

My opinion of the various clinics and my recommendations follow. It should be understood, however, that in judging the efficiency of the clinics the same criteria cannot be applied in every instance and that the classification between "excellent" and "good" is arbitrary.

APPROVED CLINICS

Excellent Clinics

Beverly

Fall River. This clinic is approved in spite of the facts that there are three large hospitals in the city and that the patients from the Truesdale Hospital are not seen in the clinic.

Gardner.

Lowell.

Lynn.

Pondville Hospital.

Salem.

Westfield Sanatorium.

Worcester.

Good Clinics

Boston—Beth Israel Hospital.

Boston Dispensary. This is a consultation clinic only.

Fitchburg.

Gloucester. This clinic is small, but much interest in it is being shown by the local medical profession.

Lawrence.

New Bedford.

North Adams. This is a very small clinic, but the committee is attempting to build it up.

CLINICS SUBJECT TO CRITICISM

Brockton. This appears to be an active clinic held at the Brockton Hospital, but certain of the men in charge of the clinic are not on the staff of that hospital; this fact hampers their efficiency. The attendance has fallen off half since 1935, and it does not appear to have the support of the local practitioners. It is apparently not uncommon for physicians to telephone the social worker, asking her if it is possible for a patient to be admitted

to the Pondville Hospital without passing through the clinic. It seems unfortunate to discontinue a clinic in as large a center as Brockton, but unless more interest is shown by the local members of the profession in the future, this should be considered and patients referred directly to Pondville Hospital, which is relatively near.

Greenfield. This clinic has been discontinued twice (in 1933 and 1941) since it was first opened. It was reopened in 1942, and recommendations for its conduct were drawn up by a committee appointed by the president of the Hampden District Medical Society. This committee was then discharged, and one to conduct the clinic appointed, consisting of one man from Greenfield, one from Montague and one from Shelburne Falls. These men are all busy and find it difficult to give up the time to attend the clinic. None were present on the day of my visit, but I finally interviewed the chairman in Montague. So little interest is shown that I believe this clinic should be again discontinued.

Hyannis. The clinic is administered by one person and is small, considering the size of the territory served. The budget is relatively large (Table 2). Considering its geographical situation, it is probably necessary to continue it, but it should be reorganized, if possible.

Newburyport. There are many excellent practitioners in the city, but no surgeon or radiologist and no one with a special interest in cancer. In cases of suspected cancer, private consultations are usually obtained. The clinic is small, serving 25 new patients in 1941, of whom 6 had cancer. The budget, however, is also small—\$300. I believe this clinic should be discontinued.

Pittsfield. This clinic, although situated in the center of Berkshire County, is not patronized by the local profession, who refer their patients directly to Westfield or Albany. Only 10 new patients were seen in 1941, and on the day of my visit there were no patients. Of the 42 patients with cancer from the Pittsfield district examined at the state clinics in 1941, 40 were first examined in Westfield. The unit cost per visit is higher than that in any other clinic—\$6.61. This clinic should be reorganized or discontinued. (The Department of Public Health is investigating the situation in Pittsfield at the present time.)

Quincy. This is a small clinic and is not patronized by the physicians in Quincy or the adjacent towns, who usually obtain a private consultation or refer their patients to one of the Boston clinics. Three new cases of cancer were seen at the clinic in 1941. I suggest that this clinic be discontinued. (Since the above was written the Department of Public Health has received a letter from the committee in charge of this clinic suggesting that it be discontinued.)

Springfield. There is a lack of interest shown by the physicians of the city in the clinic, and it does not appear to function in a satisfactory manner. Only 12 per cent of the cases of cancer from Springfield consulting the state cancer clinics are first seen in this clinic. Springfield is seven miles from the Westfield Sanatorium, and there are good transportation facilities. I believe the clinic should be discontinued.

CHANNING C. SIMMONS, M.D.

REPORT OF COMMITTEE ON CANCER

In accordance with the vote of the Council, requested by this committee in May, the President appointed Dr. Channing C. Simmons to investigate and report on the state-aided cancer clinics. This report has been presented to the secretary of the Society, and the Committee on

Cancer makes the following comments and recommendations based on it

The Committee desires to commend the diligence, effort and thought that have gone into the preparation of Dr. Simmons's report. Only one with his long experience in the cancer field could grasp the many problems and assay the work that is being done

It gives great satisfaction to the committee to realize from this report the excellent work that is being done here. The State by the members of the Society in the field of cancer. The wholehearted co-operation of the medical profession with the Department of Public Health in this field has done much to make Massachusetts the leading state in cancer control

Several facts are apparent both from Dr. Simmons's report and from general experience

The mere existence of a cancer clinic in the community is useful, entirely apart from its own work, in bringing to the minds of laymen and physicians alike the problems connected with cancer, its diagnosis and its treatment. This indirect value of the state-aided cancer clinic to the community in which it is located is a factor that must be kept in mind in evaluating the work of any specific clinic and in weighing the advantage to the community as a whole of its continuance or discontinuance

The committee is well aware that at times the two state cancer hospitals, with their outpatient clinics, may appear to encroach on the field of nearby diagnostic cancer clinics. However, it is the opinion of this committee, as it is of the Department of Public Health and the staffs of the state cancer hospitals, that there should be no such encroachment, and every effort is being made to prevent it. The function of the cancer hospitals and their outpatient clinics is to supplement rather than to supplant the state-aided diagnostic clinics

With the difficult times ahead, when transportation becomes more and more a problem, the value of the regional distribution of the state-aided cancer clinics will become more and more apparent

To those members of the medical profession who have given their time and effort over the years to the carrying on of these clinics, the Society as a whole and every citizen of the State owe a debt of gratitude

Dr. Simmons's report is largely based on the viewpoint of service to patients. That, in the last analysis, is the yardstick by which the accomplishment of the clinics must be measured. However, other criteria must be employed: the indirect value of the clinic in the community, the role that it may play with the changing conditions of war, and the value that it may have under difficult conditions of transportation. The value of the clinic as a center of postgraduate education in cancer must also be given serious consideration

On the other hand, one must consider the increasing proportion of money flowing into the war effort and related fields, and the expenditures of the clinics must be carefully weighed against their utility to their communities and to the State

Considering Dr. Simmons's report as a whole in its relation to these facts, the Committee on Cancer presents to the Council the following recommendations

That the Council thank Dr. Simmons for his services

That it is advisable to suggest to the Department of Public Health the maintenance of existing clinics with the following exceptions: the state-aided clinics at Quincy and at Newburyport should be discontinued

That particular study be made of the clinics in Brockton, Greenfield, Pittsfield, Springfield and Hyannis to

determine whether they can be more active and of greater service to their communities (The physicians in these communities are now being interviewed to obtain their opinions of the clinics and their suggestions)

SHIELDS WARREN, MD, *Chairman*

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY SEPTICEMIA AND DEATH FOLLOWING INTERNAL PODALIC VERSION

A twenty four year old primipara, who had had adequate and intelligent prenatal care, when about five months pregnant developed pyelitis, which subsided with treatment and did not recur. The past history was irrelevant. Labor began at term after spontaneous rupture of the membranes, and a forceps delivery was attempted after full dilatation. Since the position was posterior and the head could not be rotated, an internal podalic version was done. At the time of this procedure, the cord was not pulsating. The third stage of labor, after delivery of a stillborn infant, was uncomplicated. On the day after delivery, the temperature rose, and in spite of two transfusions and sulfanilamide therapy, the patient died of septicemia ten days after delivery. Several blood cultures were reported to be negative. Autopsy revealed post partum endometritis, with septicemia and early general peritonitis.

Comment It is unfortunate that the ineptness of the operator resulted in an unsuccessful forceps delivery. Undoubtedly, a trained obstetrician could have successfully delivered this patient without resorting to internal podalic version, which was performed after it was known that the fetus was not viable. It is probable, although not necessarily so, that the trauma of the internal podalic version was an element in the subsequent sepsis. When the fetal heart has ceased to pulsate, it is probably much better obstetrics to do a craniotomy than to resort to internal podalic version, a more difficult procedure.

This fatality occurred before sulfanilamide therapy had been intelligently worked out, and it quite possibly was not given so effectively then as it would be now. In spite of the fact that all blood cultures were reported to be negative, there is no evidence that a culture from the uterus was taken as a basis for sulfanilamide therapy. Sepsis may well occur without any operative procedure as a causative factor. It is too much to hope that chemotherapy will prevent such obstetric fatalities, but certainly intelligent chemotherapy combined with immune transfusions will reduce the rate very materially.

DEATHS

JACKSON — OLIVER H. JACKSON, M.D., of Fall River, died June 1. He was in his seventy-first year.

Dr. Jackson received his degree from Long Island College of Medicine in 1894. He was ophthalmologist at the Union and St. Anne hospitals and consulting ophthalmologist at the Fall River General Hospital. He was a member of the American Laryngological, Rhinological and Otological Society, the New England Ophthalmological Society and the New England Otological and Laryngological Society, and a fellow of the American College of Surgeons, the Massachusetts Medical Society and the American Medical Association.

O'TOOLE — JOHN L. O'TOOLE, M.D., of Haverhill, died September 2. He was in his sixty-fifth year.

Dr. O'Toole received his degree from Tufts College Medical School in 1908. He was medical examiner for the fourth district of Essex County, and a former member of the Massachusetts Medical Society and the American Medical Association.

WALSH — CHARLES J. WALSH, M.D., of Gilbertville, died September 6. He was in his eighty-fourth year.

A native of Barre, Dr. Walsh received his degree from College of Physicians and Surgeons, Baltimore, in 1893. He was a member of the Massachusetts Medical Society and the American Medical Association.

A brother and two sisters survive him.

WAR ACTIVITIES

PROCUREMENT AND ASSIGNMENT SERVICE

The Directing Board of the Procurement and Assignment Service for Physicians, Dentists, and Veterinarians, has recently adopted a formal resolution expressing its appreciation of the services rendered by Lieutenant Colonel Sam F. Seeley, who has been transferred to military duty. The text of the resolution is as follows:

The transfer of Lieutenant Colonel Sam F. Seeley from his connection with the Procurement and Assignment Service to active military duty causes a great loss. Lieutenant Colonel Seeley, who has acted as executive officer since the beginning of this service, has been transferred to military duty, which is in keeping with the policy recently adopted by the War Department. His training and experience with the Medical Corps of the Army in his professional capacity amply justify such a step.

The Directing Board of the Procurement and Assignment Service wishes to take this opportunity of expressing to the Surgeon General of the United States Army its very deep appreciation for the valuable service that Lieutenant Colonel Seeley has rendered during its period of organization and functions.

The Directing Board expresses to Lieutenant Colonel Seeley its deep appreciation for the great sacrifice that he has made in dislocating himself from actual military duty to serve with us in an executive capacity. He has been most unselfish, and has given unstintingly of his time, energy and patience in helping to solve many of the problems connected with the functioning of the

Procurement and Assignment Service. He has not only labored faithfully at our office in Washington, but he has traveled over the United States, making contact with many of his professional conferees and explaining to them the purpose for which the Procurement and Assignment Service was organized. His services have been most valuable and have helped to take us a long way in accomplishing the objectives for which the service was created.

The Directing Board expresses to Lieutenant Colonel Seeley its gratitude and thanks for his unselfish devotion to the organization of the Procurement and Assignment Service and wishes for him the greatest success in his new assignment.

FRANK H. LAHEY, M.D., *Chairman*

HARVEY B. STONE, MD

HAROLD S. DIEHL, MD

JAMES E. PAULLIN, MD

C. WILLARD CAMALIER, D.D.S.

MISCELLANY

PEPTIC-ULCER FILM AVAILABLE

The first complete motion-picture film on peptic ulcer, in color and with a sound track, is now available for showings before groups of physicians. The film is entitled "Peptic Ulcer" and was produced under the direction of the Department of Gastroenterology of the Lahey Clinic, Boston. The American College of Surgeons has awarded its seal of approval to the film. The running time is forty-five minutes, and the film covers a presentation of the following problems of peptic ulcer: pathogenesis, diagnosis, treatment, pathology, complications, including obstruction, hemorrhage and perforation, and gastric ulcer and jejunal-ulcer surgery.

Arrangements for a showing of the film before medical groups may be made by writing to the Professional Service Department, John Wyeth and Brother, Incorporated, Philadelphia, who will provide projection equipment, screen, film and operator, without charge.

NOTES

It is with great regret that the *Journal* records the death of Helen Matilda Bowers, wife of Dr. Walter P. Bowers, managing editor of the *Journal* for many years. Mrs. Bowers, who was eighty-five years old, had been in poor health for several years and had been confined to her home in Clinton.

The appointment of Dr. Roy D. Halloran, superintendent of the Metropolitan State Hospital, Waltham, Massachusetts, as chief of the Neuropsychiatric Division of the United States Army, with the rank of colonel, has recently been announced. Assigned to the Surgeon General's Office, Dr. Halloran will co-ordinate neuropsychiatric services in the Army, both in this country and overseas. He assumed his new duties on August 17.

Dr. Henry A. Christian, Hersey Professor of the Theory and Practice of Physic, Emeritus, has been invited by the President and Fellows of Harvard University to return to active duty to give clinical instruction; he has also been appointed visiting physician at the Beth Israel Hospital, Boston.

(Notices on page ix)

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SULFONAMIDE THERAPY IN GONOCOCCAL INFECTION IN WOMEN AND CHILDREN*

Sulfanilamide, Sulfapyridine, Sulfathiazole and Sulfadiazine

FRED L. ADAIR, M.D.,† AND LUCILE R. HAC, PH.D.‡

CHICAGO

THE value of sulfonamide therapy in gonococcal infection has been well established. Nevertheless, the present emergency has proved that gonorrhea is still a serious problem for the armed forces. According to data prepared by the office of the Surgeon General of the United States Army,¹ the year 1939 marked the lowest annual rate for admissions for venereal diseases; the rate dropped sharply in 1918 and 1919, gradually decreased almost year by year after 1922 and rose in 1940 with the increase in the Army, but was still below that of 1919. Some 60,000 selectees and volunteers were deferred because they showed evidence of venereal disease.

The increase in the total rate of venereal disease was largely due to a 50 per cent increase in the incidence of gonorrhea. There were more than 4 cases of gonorrhea to each case of syphilis. According to Rose, Kendell and Simpson:²

The antiquity, the inconspicuousness and the false sense of innocuousness all have combined to mask the real import of the havoc wrought by venereal diseases in the theaters of military and naval operations. In military and army parlance a casualty includes any officer or enlisted man rendered noncombatant as a result of death, wounds, illness, discharge, capture or desertion. During the first World War there were 100,000 more new cases of venereal diseases than there were war wounds in battle. Hence, the venereal infection ranks high in the production of casualties.

It is not practical to review the literature on the treatment of gonorrhea. Suffice it to say that the literature on the treatment in men is voluminous, the reports on women are fewer, and the results conflicting and confusing. It is gen-

erally conceded that professional prostitutes are the principal carriers of this infection, although the *Lancet*³ asserts that "even in country districts the vicious amateur forms a dangerous focus of disease and remains impervious to reason and education."

The part women play in the spread of this infection, therefore, makes it almost imperative that their treatment be accurately evaluated. It is essential to determine to what therapy women respond most readily, whether they harbor the organism over long periods with few or no symptoms, when they cease to be carriers and whether so-called "drug fast strains" are frequently produced.

It has been our purpose to study a sufficiently large series of women treated with each of the sulfonamides to be able to draw accurate conclusions concerning the best methods of diagnosis and treatment, and to determine the drug of choice and the necessary criteria of cure of this infection.

MATERIALS AND METHODS

In this study of 453 women and 80 children who received chemotherapy, all the patients were ambulatory. Cure was based on routine cultures and smears. Four sulfonamides—sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine—were used. An attempt was made to assign the patients in rotation to the various drugs. Because sulfadiazine has been used only a short time, the series is smaller than those of the other drugs.

Classification of Patients

A total of 587 women received treatment, but 108 unco-operative patients were omitted because they could not be observed longer than one month. Of the remaining 453 patients, 145 became re-

*Presented at the annual meeting of the New Hampshire Medical Society, Manchester, May 13, 1942.

†From the Department of Obstetrics and Gynecology, University of Chicago, and the Chicago Lying-in Hospital.

‡This work was done under a grant from the Albert B. Kupperheimer Foundation, University of Chicago.

†Mary Campau Ryer, Professor and chairman, Department of Obstetrics and Gynecology, University of Chicago, and chief of staff, Chicago Lying-in Hospital.

‡Resident instructor, Department of Obstetrics and Gynecology, University of Chicago.

Most of the patients in this study were made available through Dr. H. N. Bunsen of the Chicago Board of Health and Drs. G. G. Taylor and D. A. Hibbs, of the Municipal Social Hygiene Clinic of Chicago.

The sulfonamides used in this study were kindly furnished through the courtesy of the Department of Medical Research, Winthrop Chemical Company, New York City (sulfanilamide and sulfathiazole), Merck and Company, Rahway, New Jersey (sulfapyridine) and Lederle Laboratories, Incorporated, Pearl River, New York (sulfadiazine).

infected during the two-month observation period that followed therapy. We believe that these patients suffered two or more infections and have, therefore, designated *each infection* as a *case*, regardless of whether the patients received previous therapy. Accordingly, one patient might constitute two or more cases, making a total of 604 cases in all. Of these, 155 received sulfanilamide, 222 sulfapyridine, 166 sulfathiazole and 61 sulfadiazine.

Eighty children received a total of one hundred and five courses of treatment.* Fifty-four children received one course of therapy, 8 two courses,

TABLE 1. *Sulfonamide Dosage in Ambulatory Cases of Gonococcal Infection in Women.*

DRUG	DAILY DOSAGE*	NO. OF DAYS	TOTAL NO. OF DAYS	TOTAL DOSAGE
	gm.			gm.
Sulfanilamide	4 (60 gr.) 2.6 (40 gr.)	4 10	14	42 (630 gr.)
Sulfapyridine and sulfathiazole	3 (45 gr.) 2 (30 gr.)	2 4	6	14 (210 gr.)
Sulfadiazine	2 (30 gr.)	6	6	12 (180 gr.)

*Divided into four equal doses.

6 three courses, 3 four courses, and 1 five courses. Of these, 15 received sulfanilamide, 49 sulfapyridine, and 41 sulfathiazole. Stilbestrol was used in the treatment of children who did not respond to sulfonamide therapy.

Treatment

Table 1 gives the dosage schedule for adults, and Table 2 that for children. Patients who did not respond favorably to treatment and those who were reinfected received a second course of the same drug or were shifted to another drug after an interval of three to seven days without therapy.

The plan of procedure in the study of the patients has been outlined in detail in a previous publication.⁴ Diagnosis in every case was based

TABLE 2. *Dosage of Sulfapyridine, Sulfathiazole and Sulfadiazine in Ambulatory Cases of Gonococcal Infection in Girls.*

AGE	WEIGHT	DAILY DOSAGE*	NO. OF DAYS	TOTAL DOSAGE
yr.	lb.	gm.		gm.
1-2	20-26	0.75 (11 gr.)	10	7.5 (113 gr.)
2-5	27-41	1.5 (23 gr.)	10	15.0 (225 gr.)
5-9	42-61	2.0 (30 gr.)	10	20.0 (300 gr.)
9-11	62-100	2.5 (38 gr.)	10	25.0 (375 gr.)

*Approximately 0.75 gm. per 20 lb. (9.1 kg.) daily, divided into four equal doses.

on the isolation of the gonococcus in culture. The criteria of cure required that patients remain negative through two menstrual periods and two

postmenstrual provocative tests. Patients who did not menstruate were observed for two months, and received two provocative tests.

Smears and cultures were taken two or three times a week during treatment. After the first negative culture was obtained, smears and cultures were taken twice a week for the first month and at least once a week thereafter. They were also taken during and just following the menstrual period. The provocative test, which consisted of the application of 10 per cent silver nitrate to the cervix and 5 per cent silver nitrate to the urethra, was performed on the first or second postmenstrual day of each period, and cultures were taken on that day, and the first and fourth days subsequently. Children were checked during treatment and for the following month by cultures and smears taken twice weekly, then weekly for two months and monthly thereafter until they had been observed for a year; no provocative test was used. Blood for the determination of the drug concentration was taken once or twice during therapy.

RESULTS

Table 3 presents the results of treatment. Those cases designated as cures were observed through two negative menstrual periods followed by negative provocative tests. The failures occurred in cases from which evidence of reinfection could

TABLE 3. *Efficacy of Sulfonamides in the Treatment of Gonococcal Infections in Women.*

	SULFANIL-AMIDE		SULFAPYRI-DINE		SULFATHIA-ZOLE		SULFADIA-ZINE	
	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT
Cures	81	52	108	49	108	65	46	75
Delinquents*	12	8	29	13	5	3	4	7
Reinfections	37	34	67	30	45	27	9	15
Failures	25	16	18	8	8	5	2	3
Totals	155		222		166		61	

*Negative more than one month and probably cured.

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All the delinquent cases were negative for more than a month and were probably cured, but since further observation was impossible, they have been deleted from Table 4.

In cases considered probable reinfections, the patients either had spermatozoa in the smears or admitted sexual contact. The recurrence of positive findings was due either to reinfection or to exacerbation of a latent infection. We believe that most of these cases must have been reinfections, but since it cannot be proved, we have deleted the cases from Table 4 rather than class them as cured cases that had been reinfected, or as definite fail-

res It is our impression, however, that in series of well controlled and checked, such cases might be considered drug failures

In Table 4, with the delinquent cases and probable reinfections deleted, 24 per cent of the cases

TABLE 4 Final Comparison of Results of Sulfonamide Therapy in Women *

	SULFANILAMIDE		SULFAPYRIDINE		SULFATHIAZOLE		SULFADIAZINE	
	NO OF CASES	PER CENT	NO OF CASES	PER CENT	NO OF CASES	PER CENT	NO OF CASES	PER CENT
Cures	81	76	103	86	103	93	46	96
Failures	25	24	18	14	8	7	2	4
Totals	106		126		116		48	

*Delinquents and reinfections deleted

that received sulfanilamide, 14 per cent that received sulfapyridine, 7 per cent that received sulfathiazole, and 4 per cent that received sulfadiazine were drug failures The outcome of these failures is given in Table 5.

In this group of 453 women, there were 44 pregnant patients, of whom 6 were reinfected but were cured on subsequent treatment; 8 with repeated reinfections were deleted from the series Three pregnant patients were discharged cured by sulfanilamide, 8 by sulfapyridine, 20 by sulfathiazole

41 (24 per cent) children were drug failures; 5 had failed to respond to previous sulfonamide therapy. One drug-fast strain was produced All the children in whom drug-fast strains were produced were treated and cured with stilbestrol or a combination of stilbestrol and sulfonamide therapy *

Blood Concentration

Blood concentrations as high as 10 mg. per 100 cc. were obtained in patients who received sulfanilamide, but most of them were between 3 and 4 mg. per 100 cc. With sulfapyridine and sulfathiazole, the highest levels were 8 mg. per 100 cc., most of them being between 2 and 3 mg. With a 2 gm. daily dose of sulfadiazine, the concentration in the blood was usually between 4 and 6 mg. per 100 cc. Earlier, when a 3 gm. daily dose was used, levels between 8 and 11 mg. per 100 cc. were frequent These seemed unnecessarily high and might be dangerous in ambulatory patients. For that reason, the daily dose of sulfadiazine was lowered to 2 gm. There was no increase in the number of failures with this lower dose

Toxicity

A large number of patients who received sulfanilamide and sulfapyridine exhibited minor toxic symptoms. The number of toxic symptoms with

TABLE 5 Outcome of Failures of Sulfonamide Therapy in the Treatment of Gonococcal Infections in Women

SULFANILAMIDE 25 CASES	SULFAPYRIDINE 18 CASES	SULFATHIAZOLE 8 CASES	SULFADIAZINE 2 CASES
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In gonococcal vulvovaginitis, 13 of 15 (89 per cent) children who received sulfanilamide were drug failures, and 5 drug-fast strains were produced With sulfapyridine, 12 of 49 (25 per cent) children were failures—5 of these had previously been failures with sulfanilamide Two drug-fast strains were produced With sulfathiazole, 10 of

sulfadiazine was about as great as that with sulfathiazole, but both drugs were better tolerated than sulfanilamide or sulfapyridine. Very rarely was it necessary to discontinue treatment because of toxic symptoms.

DISCUSSION

It has been shown that diagnosis and cure of gonococcal infection must be based on cultures rather than smears⁶ In a study of 216 patients with one thousand six hundred and seventy five cultures, over 50 per cent of the positive cultures had corresponding negative smears Moreover, many patients showed persistently positive cultures, although the smears were consistently negative Conversely, only 0.5 per cent of the positive smears had corresponding negative cultures

*The dose of stilbestrol was as follows: 0.1 mg. three times a day for thirteen to twenty days

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DISCUSSION

It has been shown that diagnosis and cure of gonococcal infection must be based on cultures rather than smears.⁵ In a study of 216 patients with one thousand six hundred and seventy five cultures, over 50 per cent of the positive cultures had corresponding negative smears. Moreover, many patients showed persistently positive cultures, although the smears were consistently negative. Conversely, only 0.5 per cent of the positive smears had corresponding negative cultures.

*The dose of stilbestrol was as follows: 0.1 mg. three times a day for thirteen to twenty days.

The reliability of initial diagnosis or of cure, whether on the basis of smear or culture, is largely dependent on the technic used in the collection of material. Good smears are unquestionably more difficult to obtain in women than in men, but with care they can be prepared quite easily. The material must be taken from sites that harbor the gonococcus, such as Skene's, Bartholin's and the endocervical glands. Material from the vagina or the vaginal introitus rarely contains gonococci after subsidence of the acute stage of the infection. Moreover, material from this area is usually so badly contaminated with vaginal bacteria that the slides are unreadable and the cultures are overgrown.

The meatus of the urethra should be wiped dry with a piece of cotton to avoid inclusion of confusing vulval bacteria. The finger should then be passed within the vagina, and the urethra firmly stripped from above downward against the pubic arch. A cotton swab may be used for collection of the material.

To obtain satisfactory specimens from the cervical glands, the cervix should be exposed with a speculum inserted without lubrication other than water. The vaginal secretion should be wiped out, and the plug of cervical mucus mechanically removed. The cervix should then be compressed with the speculum, to force the secretion from the endocervical glands, and the material removed on a cotton swab inserted directly into the cervical canal. Some workers prefer to insert the swab and then compress the cervix with the speculum.

The great discrepancy between positive cultures and smears has led us to try various methods for collection of the material. With smears prepared from swabs as compared with those prepared with a platinum loop, we obtained more positive slides with swabs than with loops, although the pus cells in smears made with the loop were less distorted than those made with swabs.

A comparison of the results of cultures taken during and just following the menstrual period indicates that occasionally a positive culture is obtained during the menstrual period and not postmenstrually, but the number is hardly large enough to warrant the procedure, since most patients object to visits during the period. Postmenstrual smears and cultures, however, are quite essential. Frequently, positive results are obtained at this time and at no other time.

A comparison of the results of cultures taken following the menstrual period with the results obtained after a provocative test with silver nitrate has convinced us that the menstrual period is the best provocative test of cure of gonococcal infection

in women. Cultures taken the first day after the provocative test, as is the usual custom, may lead to erroneous conclusions. We have had a small series of patients who had positive cultures on the postmenstrual day, the day on which the provocative test was done. Although positive cultures were again obtained on the fourth postprovocative day, the cultures taken on the first postprovocative day were negative. Therefore, if a provocative test is done, cultures taken on the third or fourth day after the test rather than the first day are better criteria of cure. These data will be published later.

Previously, we had required that patients be observed through three negative menstrual periods and provocative tests before they could be discharged as cured, but in 235 patients, only 2 patients who gave no evidence of reinfection became positive during the third month of observation. Both became delinquent, and further information to substantiate the evidence of drug failure could not be obtained. It seems, therefore, that observation through two menstrual periods is sufficient.

The results with sulfonamide therapy in women lead to the conclusion that sulfathiazole (93 per cent cure) and sulfadiazine (96 per cent cure) are the drugs of choice for the treatment of gonorrhea in women. Sulfapyridine gives quite good results (86 per cent cure), but patients complain of minor toxic symptoms more frequently than they do with sulfathiazole or sulfadiazine. An occasional case that has been a failure with sulfathiazole responds to sulfapyridine. Sulfanilamide is definitely better than local treatment, but it is the poorest (76 per cent cure) of the sulfonamide compounds studied. Moreover, it requires larger doses for a longer time than the other compounds do. Response to treatment is more rapid with sulfathiazole and sulfadiazine than with sulfanilamide. With sulfanilamide, 88 per cent of the patients who were cured had negative cultures within four days after treatment was begun. With sulfapyridine, 93 per cent; with sulfathiazole, 97 per cent; and with the small series of sulfadiazine patients, 98 per cent of the cultures were negative within four days. Women, therefore, respond rapidly to sulfonamide therapy. In a previous series of patients who received local therapy (2 per cent Mercurochrome), there were only 80 per cent failures after six weeks of treatment.⁴

Only relatively small doses of the sulfonamides are necessary for cure. We believe that the high percentage of cures in our series has been dependent somewhat on the low dosage of drugs given. Patients are better able to tolerate small

amounts of the drug. They are more willing to take the drug and are better able to retain it than when large doses are given.

With the sulfonamides, secondary complications are relatively rare if therapy is begun early.

Drug fast strains are not readily produced in women. In our series of 453 patients, only 1 patient gave evidence of so-called "drug-fastness," and she became delinquent, so that definite proof was lacking. Not infrequently, we have had patients who were supposed failures with all the drugs, but careful check has always shown that this was due to reinfection and not to drug fastness of the particular strain of the gonococcus.

Our series of pregnant patients is too small to permit definite conclusions. The 12 per cent failure rate is somewhat higher than that in the nonpregnant group. It is possible that, as in certain other infections, gonorrhea may be more resistant to treatment during pregnancy. Two of the 5 patients who were drug failures in this group failed to respond to treatment until the post partum period. All the patients were checked post partum. None of the infants developed the infection, and none of them seemed to have been adversely affected by the treatment during pregnancy.

Gonorrhea in children is more difficult to diagnose and to control than in adults. Cultures are not quite so reliable as in adults, and smears are much more liable to error, primarily because other cocci present in the vagina may be confusing. It is essential that smears be carefully stained (by Gram's method) and controlled to avoid over decolorization.

Children require larger doses of sulfonamides for a longer time than adults do. Previous studies indicated that a ten day course of treatment is the minimum in children, and at least 0.75 gm per 20 pounds of body weight should be the minimum dose with sulfapyridine and sulfathiazole. So far, too few patients have received sulfadiazine for us to know whether or not the dose may be lowered.

Sulfanilamide is definitely contraindicated in the treatment of children because it tends to produce drug fast strains, hence so few cases in this series. Sulfapyridine and sulfathiazole are about equally effective, but sulfathiazole produced fewer minor toxic symptoms. The occasional drug-fast strain has responded to treatment with stilbestrol or a combination of stilbestrol and sulfonamide therapy, but since we have discontinued

the use of sulfanilamide we have encountered only three such strains.

We have had considerable difficulty in determining whether or not some of the children had become reinfecting or were failures. In no case in which we were certain that the recurrence was due to a failure has that recurrence taken place after the third month following therapy. Three months, therefore, is probably long enough to check children before they are discharged as cured.

SUMMARY AND CONCLUSIONS

Sulfonamides were used in the treatment of gonococcal infection in 453 women and 80 children.

Diagnosis and cure should be based on cultures as well as smears.

Patients should be observed through two negative menstrual periods before they are discharged as cured.

Sulfathiazole and sulfadiazine are the drugs of choice for the treatment of women. The rate of cure with sulfanilamide was 76 per cent, with sulfapyridine 86 per cent, with sulfathiazole 93 per cent and with sulfadiazine 96 per cent.

Women respond rapidly to sulfonamide therapy and become noncontagious much earlier than when local treatment is used. Of those cured with sulfathiazole, 97 per cent had negative smears and cultures within four days after treatment was begun; with sulfadiazine, 98 per cent responded within four days.

Secondary complications are rare if sulfonamides are administered early. None of the patients discharged as cured required surgical treatment for complications.

Drug fast strains of gonococci are produced extremely rarely in women: 1 in 453 patients.

Sulfathiazole is the drug of choice in the treatment of vulvovaginitis in children. Sulfanilamide is contraindicated.

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The reliability of initial diagnosis or of cure, whether on the basis of smear or culture, is largely dependent on the technic used in the collection of material. Good smears are unquestionably more difficult to obtain in women than in men, but with care they can be prepared quite easily. The material must be taken from sites that harbor the gonococcus, such as Skene's, Bartholin's and the endocervical glands. Material from the vagina or the vaginal introitus rarely contains gonococci after subsidence of the acute stage of the infection. Moreover, material from this area is usually so badly contaminated with vaginal bacteria that the slides are unreadable and the cultures are overgrown.

The meatus of the urethra should be wiped dry with a piece of cotton to avoid inclusion of confusing vulval bacteria. The finger should then be passed within the vagina, and the urethra firmly stripped from above downward against the pubic arch. A cotton swab may be used for collection of the material.

To obtain satisfactory specimens from the cervical glands, the cervix should be exposed with a speculum inserted without lubrication other than water. The vaginal secretion should be wiped out, and the plug of cervical mucus mechanically removed. The cervix should then be compressed with the speculum, to force the secretion from the endocervical glands, and the material removed on a cotton swab inserted directly into the cervical canal. Some workers prefer to insert the swab and then compress the cervix with the speculum.

The great discrepancy between positive cultures and smears has led us to try various methods for collection of the material. With smears prepared from swabs as compared with those prepared with a platinum loop, we obtained more positive slides with swabs than with loops, although the pus cells in smears made with the loop were less distorted than those made with swabs.

A comparison of the results of cultures taken during and just following the menstrual period indicates that occasionally a positive culture is obtained during the menstrual period and not postmenstrually, but the number is hardly large enough to warrant the procedure, since most patients object to visits during the period. Postmenstrual smears and cultures, however, are quite essential. Frequently, positive results are obtained at this time and at no other time.

A comparison of the results of cultures taken following the menstrual period with the results obtained after a provocative test with silver nitrate has convinced us that the menstrual period is the best provocative test of cure of gonococcal infection

in women. Cultures taken the first day after the provocative test, as is the usual custom, may lead to erroneous conclusions. We have had a small series of patients who had positive cultures on the postmenstrual day, the day on which the provocative test was done. Although positive cultures were again obtained on the fourth postprovocative day, the cultures taken on the first postprovocative day were negative. Therefore, if a provocative test is done, cultures taken on the third or fourth day after the test rather than the first day are better criteria of cure. These data will be published later.

Previously, we had required that patients be observed through three negative menstrual periods and provocative tests before they could be discharged as cured, but in 235 patients, only 2 patients who gave no evidence of reinfection became positive during the third month of observation. Both became delinquent, and further information to substantiate the evidence of drug failure could not be obtained. It seems, therefore, that observation through two menstrual periods is sufficient.

The results with sulfonamide therapy in women lead to the conclusion that sulfathiazole (93 per cent cure) and sulfadiazine (96 per cent cure) are the drugs of choice for the treatment of gonorrhea in women. Sulfapyridine gives quite good results (86 per cent cure), but patients complain of minor toxic symptoms more frequently than they do with sulfathiazole or sulfadiazine. An occasional case that has been a failure with sulfathiazole responds to sulfapyridine. Sulfanilamide is definitely better than local treatment, but it is the poorest (76 per cent cure) of the sulfonamide compounds studied. Moreover, it requires larger doses for a longer time than the other compounds do. Response to treatment is more rapid with sulfathiazole and sulfadiazine than with sulfanilamide. With sulfanilamide, 88 per cent of the patients who were cured had negative cultures within four days after treatment was begun. With sulfapyridine, 93 per cent; with sulfathiazole, 97 per cent; and with the small series of sulfadiazine patients, 98 per cent of the cultures were negative within four days. Women, therefore, respond rapidly to sulfonamide therapy. In a previous series of patients who received local therapy (2 per cent Mercurochrome), there were only 80 per cent failures after six weeks of treatment.⁴

Only relatively small doses of the sulfonamides are necessary for cure. We believe that the high percentage of cures in our series has been dependent somewhat on the low dosage of drugs given. Patients are better able to tolerate small

infection without stones. Two patients had the so-called "postcholecystectomy syndrome." All the 11 patients with common duct involvement had jaundice; the remaining 7 were not jaundiced. Eight patients gave a history of colic shortly before admission.

Nine patients had electrocardiographic abnormalities on admission to the hospital. In 6 out of 7 of these patients, the carotid sinus reflex was found to be insensitive when re-examined postoperatively or after the jaundice had subsided. This observation makes pre-existent myocardial disease—that is, disease of the effector organ—unlikely as the major factor in the production of the reaction. Whether there were other functional factors affecting the myocardium cannot be stated. Unfortunately, it is not known whether the electrocardiographic abnormalities also disappeared, but other observers have noted a return of the electrocardiogram toward normal in similar patients after operation.⁹ The electrocardiographic changes included sinus bradycardia, prolonged PR interval, notching and slurring of the QRS complexes, RT depressions and T-wave inversions. In 2 cases, the bradycardia was striking, a rate of 40 to 45 per minute being a prominent feature. Both patients were jaundiced. In 1 case, changes suggestive of an anterior-wall myocardial infarction developed after abdominal pain and icterus had subsided; the clinical course and x-ray findings suggested that common duct obstruction, which was apparently spontaneously relieved, was followed by myocardial infarction, presumably due to acute coronary occlusion. Two patients showed auricular fibrillation, which was paroxysmal in 1 and coincided with an episode of acute biliary colic. Six of the patients who showed electrocardiographic changes also presented evidence of varying degrees of arteriosclerosis involving the major vessels.

The carotid sinus reflex was re-examined postoperatively or after the acute symptoms had subsided in 10 of the 18 patients. In 6, the hypersensitive reflex disappeared promptly. In 1 patient with carcinoma of the head of the pancreas, both jaundice and a positive reflex persisted after cholecystgastrostomy, suggesting that the obstruction had not been completely relieved. One patient with the postcholecystectomy syndrome lost the reaction for several days when olive oil was introduced into the duodenum.

Atropine sulfate effectively blocked the cardio-inhibitory reflex in all cases in which it was tested. The subcutaneous injection of 1 mg was usually sufficient. Tincture of belladonna by mouth was also effective, but less regularly.

Seven patients had spontaneous symptoms, consisting of dizziness, faintness, sudden weakness, syncope or collapse. In 4, these symptoms occurred during acute episodes of colic; the other 3 suffered recurrent symptoms in association with ill-defined gastrointestinal complaints.

The following cases are illustrative.

CASE 1 S T, a 51-year-old man, entered the hospital because of jaundice and upper abdominal discomfort. The patient related that several weeks before admission he experienced a sudden episode of upper abdominal discomfort during which he fainted. On the following day, he noted dark urine and a light stool, and thereafter discovered that he had become jaundiced. Tarry stools were not noted.

The patient had had mild hypertension (a blood pressure of 160/100) and auricular fibrillation for several years.

Massage of the carotid sinus resulted in prolonged asystole.

Operation revealed a carcinoma of the ampulla of Vater, partially obstructing the common bile duct. Further observation could not be carried out because the patient died shortly after an attempt at resection.

CASE 2 S S, a 45-year-old man, had a cholecystectomy performed 3½ years before admission because of recurrent episodes of epigastric pain, nausea, vomiting, icterus and acholic stools. The gall bladder was found to be thickened and to contain stones, and the common duct contained chilly material. A year after operation, the patient began to have frequent bouts of pressing epigastric pain radiating up under the sternum, associated with nausea, dizziness, lachrymation, sweating, faintness and, occasionally, actual syncope. The attacks lasted about 15 minutes, and were promptly relieved by belching. Jaundice and acholic stools had not been noted.

Physical examination revealed no pertinent findings. There was no icterus. X-ray examination of the abdomen and the electrocardiogram revealed no abnormalities.

Massage of the right carotid sinus caused asystole of 5 or 6 seconds, faintness, nausea, eructation, lachrymation and, finally, syncope. The symptoms produced were identical with those occurring spontaneously, except for the absence of abdominal pain. Olive oil introduced into the duodenum by tube under fluoroscopic control resulted in a flow of bile and a loss of the carotid sinus reaction for 2 days. This was repeated on two occasions. One milligram of atropine sulfate injected subcutaneously completely abolished the carotid sinus reflex reaction. On a high fat diet and untire of belladonna by mouth, the patient noted a distinct decrease in spontaneous symptoms and the carotid sinus reflex was found to be much less sensitive.

CASE 3 D B, a 43-year-old man, was admitted to the hospital because of fainting spells occurring after meals. These were associated with upper abdominal distention, eructation and nausea, and particularly followed the ingestion of fatty foods. Jaundice or acholic stools had not occurred.

Carotid sinus massage yielded prolonged asystole, which was followed by syncope when the patient was examined in the erect position. The patient was hypersensitive to pain by the Libman test.

At operation, a thickened gall bladder containing numerous faceted stones was removed. One week after operation, it was no longer possible to elicit any carotid sinus reaction.

In Case 1, the abdominal discomfort and syncope, followed promptly by the classic signs of common-duct obstruction, suggest the possibility of sudden reflex cardiac standstill, in association with the development of the obstruction. The demonstration of a hypersensitive, cardioinhibitory carotid-sinus reflex favors the view that the vagal-reflex arc was overactive.

Cases 2 and 3 illustrate recurrent syncopal symptoms as the dominant feature of the clinical picture. The nature of the so-called "post-cholecystectomy syndrome" remains uncertain, but it is not unusual to find a greatly dilated common duct on exploration. In Case 1, there was no evidence of a persistent stone, and the absence of jaundice ruled out effective obstruction. The common duct was not involved in Case 2. It is significant that in both the therapy most effective in relieving the symptoms referable to the biliary-tract disorder also relieved the syncopal symptoms and carotid-sinus-reflex sensitivity to a similar degree.

Analysis of negative cases. Five of the 23 patients with biliary-tract disease showed no response on carotid-sinus massage. All had infection and stones in the gall bladder, and in no case was the common duct found to be involved at operation. One patient was jaundiced and may have passed a stone, but this could not be established at operation. The ages of the patients ranged from thirty-three to fifty-eight years. Two patients had biliary colic. None of the patients had any spontaneous symptoms related to syncope. Two patients had electrocardiographic changes.

Toxic Hepatitis

Thirteen proved cases of toxic hepatitis were studied, to evaluate the role of jaundice in this reaction. The patients' ages ranged from nineteen to sixty-eight years, 9 being over forty-one (Table 1). All patients were jaundiced at the time of examination. Only 1 showed a positive response to carotid-sinus massage. This was a thirty-three-year-old woman with chronic alcoholism, acute alcoholic cirrhosis, beriberi heart disease and peripheral neuritis. The carotid-sinus reaction disappeared before the jaundice had subsided. The occurrence of the cardioinhibitory type of reflex during nutritional deficiency and chronic alcoholism has been commented on by others.¹⁰ No patients had any spontaneous symptoms related to syncope. Two patients showed advanced peripheral arteriosclerosis and hypertension. Two patients had electrocardiographic changes indicating myocardial damage.

Control Cases

To obtain some idea of the incidence among the average ward population of positive reactions satisfying the criteria already described, 81 patients, of whom 55 were over forty years of age, were examined at random (Table 2). In this group,

TABLE 2. Age Incidence in Control Cases.

AGEs	NO. OF POSITIVE CASEs	NO. OF NEGATIVE CASEs
yr.		
12-20	2	3
21-30	0	11
31-40	2	8
41-50	4	17
51-60	5	17
61-70	1	8
71-80	2	1
Totals	16	65

16 patients, or 19 per cent, yielded a positive reaction. Among the 55 patients over forty years of age, positive reactions occurred in 12 cases, an incidence of 22 per cent. This incidence is identical with that observed by Sigler,¹¹ who found asystole of three seconds or more to occur in 18 per cent of 1886 patients between ten and eighty-five years of age and in 23 per cent of 1332 patients between forty and eighty-five years.

The diagnoses in the positive cases included acute rheumatic carditis, 5 cases; coronary-artery disease, 4 cases; arteriosclerosis, 2 cases; cancer of the viscera, involving peritoneum and diaphragm, 3 cases; and Graves's disease and duodenal ulcer, 1 case each.

The negative cases included the usual conditions encountered in a general hospital medical service, and were in no fashion a selected group except for the omission of several patients in whom the presence or absence of biliary-tract disease could not be established with certainty.

DISCUSSION

The pathologic factors leading to sensitization of the carotid-sinus-reflex arc are many. The production of cardiac asystole may depend on involvement of the reflex arc anywhere along its course, including the afferent and efferent pathways as well as the central synapses.¹⁰ Local disease of or around the carotid sinus, such as arteriosclerosis and neoplastic or inflammatory masses in the neck, presumably involves the afferent nerve endings or pathways. Coronary-artery and myocardial disease, particularly when the conduction system is involved as in acute rheumatic carditis, affects the efferent end of the cardioinhibitory reflex arc. Vascular or degenerative disease of the central nervous system may involve the central synapses. Other

factors, such as dietary insufficiency, menstruation and digitalis, have been noted, but the exact sites of action have not been explained.¹⁰

In the cases under consideration, it is noteworthy that the reaction occurred most frequently among the patients with common-bile-duct involvement. Increase in bile pigments in the blood is not the determining factor, as is clearly indicated by the negative results among the patients with icterus of nonobstructive origin. Whether other substances that accumulate in obstructive jaundice, particularly the bile acids and their derivatives, are concerned in this reaction is more difficult to say. Balticeano and Vasiliu^{12, 13} report that when sodium taurocholate or sodium glycocholate (0.25 to 0.5 gm.) is injected into the common carotid artery or around the carotid sinus of dogs, bradycardia and hypotension result. This reaction does not occur after denervation of the carotid sinus, after vagal section or when the material is injected distal to the carotid sinus. The positive reactions among the nonicteric patients, with subsequent recovery on subsidence of the acute episodes or after operative intervention, indicate that retention of bile salts is only one of the contributory factors and that further experimental observation is necessary to clarify this point. In the 2 patients with postcholecystectomy syndrome, both of whom had positive carotid-sinus reactions as well as spontaneous syncopal symptoms in association with gastrointestinal complaints and neither of whom had jaundice, it might be presumed that only the biliary passages were involved. It may be recalled that in 1 of these cases the introduction of olive oil into the duodenum by tube, a procedure that initiated a generous flow of bile, was followed by inability to elicit the carotid-sinus reaction for several days. When the patients without involvement of the common duct and without icterus are considered, the incidence of positive reactions is less than 50 per cent.

The evidence presented thus suggests that this phenomenon represents a summation reaction. The production of cardiac standstill in icteric animals by manipulation of the bile passages has already been commented on. In all likelihood, the asystole produced by massage of the carotid sinus does not represent an increased sensitivity of the carotid sinus itself, but results from a summation of impulses reaching the medullary centers. If impulses were to arise constantly from the distended or diseased bile passages, the addition of afferent impulses from the carotid sinus as well might then exceed the threshold of reaction of the vagal centers, with consequent cardiac inhibition. Whether there are additional factors actively influencing the heart itself is as yet unknown. The possibilities

of such indirect sensitization of a previously hypotensive cardioinhibitory reflex arc are now being investigated, and positive results have already been obtained in a number of cases. Thus, in 1 patient, the inflation of a balloon in the duodenum resulted in a complete sinus arrest, followed by an idioventricular rhythm (a rate of 45 per minute) that persisted until the tube was removed ten minutes later. For some time thereafter, although normal sinus rhythm had been restored, the slightest pressure on the carotid sinus led to a prolonged cardiac standstill. This, and similar cases, will be the subject of a more detailed report at a later date. Thus, the spontaneous reactions of bradycardia and cardiac standstill depend on a number of variable factors, any one or combination of which may be sufficient to exceed the threshold of reaction and produce symptoms. It is doubtful, however, whether the spontaneous symptoms of syncope in the cases with biliary-tract disease arise from mechanical involvement of the carotid sinus itself, except in unusual cases. It is more reasonable to suppose that the symptoms originate reflexly from impulses arising in the efferent end organs located in relation to the biliary tract. Massage of the carotid sinus simply provides a convenient means of establishing the presence of such an overactive reflex arc.

From these data, it becomes quite apparent that the finding of a hyperactive carotid-sinus reflex is evidence only of the existence of a sensitized nervous pathway, whose cause may be located anywhere along the carotid-sinus-reflex arc itself or along any one of a number of related pathways. Failure to recognize this point has led to an unfortunate overemphasis on the diagnostic and therapeutic significance of the carotid sinus itself, frequently with indifferent results. Equally misleading have been the recent attempts to attribute a greater value to the hyperactive cardioinhibitory carotid-sinus reflex than to the electrocardiogram as a diagnostic aid in coronary disease.^{11, 11} Without attempting to minimize the role of coronary disease as a sensitizing factor, one must point out that its diagnostic value is decidedly limited unless corroborative clinical or laboratory evidence is present. The greatest value of demonstrating a hyperactive carotid-sinus reflex is the attention that it directs toward certain critical points of the reflex arc that may become sensitized. Other clinical and laboratory observation may then serve to identify the underlying pathologic process responsible for this sensitization.

Comment might be made on the relation of these reflex symptoms to pain sensitivity. It is an interesting clinical observation that patients with a hypersensitive carotid-sinus reflex rarely com-

plain of pain on massage of the neck, even in the prone position, when unconsciousness usually does not occur. Libman¹⁵ has called attention to the fact that, in patients who are hyposensitive to pain, symptoms referable to the autonomic nervous system sometimes dominate the clinical picture. In 2 of the patients described in an earlier section, spontaneous symptoms of faintness, sweating, weakness and syncope clearly overshadowed the gastrointestinal symptoms. Both patients were hyposensitive to pain by the Libman test of styloid pressure. One might speculate on the possibility that the sympathetic reflexes induced by severe pain might ordinarily tend to counteract the vagal cardioinhibitory reflex, but that in the absence of the former, the vagal reflexes dominate, resulting more readily in syncope and related symptoms.

SUMMARY

The cardioinhibitory carotid-sinus reflex was examined in 23 patients with more or less acute symptoms due to biliary-tract disease, 13 patients with toxic hepatitis, and 81 ward patients selected at random.

Eighteen, or 78 per cent, of the patients with biliary-tract disease had asystole of three seconds or more on massage of the carotid sinus. Of these, 11 had common-duct obstruction and jaundice, 5 had cholecystitis and cholelithiasis, and 2 had the postcholecystectomy syndrome. In 10 patients, the carotid-sinus reflex was re-examined after the acute symptoms had subsided and was found to be negative in 6. Seven patients had spontaneous symptoms consisting of dizziness, faintness or syncope in association with symptoms referable to the biliary tract.

The 5 patients who failed to yield positive reactions had cholecystitis and cholelithiasis, without involvement of the ducts.

Among the 13 patients with toxic hepatitis, only 1 showed an overactive cardioinhibitory reflex.

Among the 81 ward patients examined at random, only 16, or 19 per cent, yielded positive reactions. The diagnoses in the positive cases included acute rheumatic carditis, coronary-artery disease, arteriosclerosis, cancer of the viscera, hyperthyroidism and duodenal ulcer.

The reaction is considered to be the result of a summation of afferent impulses and not a sensitization of the carotid sinus itself. The major portion of these impulses probably arises from afferent end organs in the region of the biliary tract, but when further impulses from the carotid sinus are added to the reflex arc, the threshold of reaction of the vagal centers is reached and cardiac inhibition ensues. The clinical significance of the hyperactive carotid-sinus reflex is discussed from the point of view of the various sites at which the reflex arc may become sensitized by disease.

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QUININE METHOCHLORIDE TREATMENT OF SPASTIC CHILDREN*

Preliminary Report

EDWARD PRESS, M D T

EAST PROVIDENCE, RHODE ISLAND

CURARE, a drug paralyzing voluntary musculature,¹ has been used successfully to reduce muscle spasm in patients with cerebral palsy,² and thereby to accelerate their treatment program. However, curare is of rather indeterminate composition, is still difficult to obtain, and is effective only when given by repeated parenteral injection. Quinine methochloride, a recently synthesized drug readily available in pure form, is said to have a curare-like action when given by mouth.^{3,4} Since it is thus free from the obvious disadvantages of curare, the present study was undertaken to determine whether it is equally effective in the treatment of cerebral palsy.

MATERIAL AND METHODS

Quinine methochloride, a white powder of low density and intensely bitter taste, is poorly soluble in water. Since some children with cerebral palsy have difficulty swallowing capsules, it was necessary to devise another method of administration. The drug dissolves only slightly in alcoholic and watery solutions, and syrups and elixirs could therefore not be used. A satisfactory method was finally devised whereby the desired amount was well dispersed in cherry syrup of thick consistence. The medicine glass was then rinsed with plain or flavored water, which the patient drank. Thus, the entire dose was given in a manner similar to that in common usage with the sulfonamide drugs in children.

The drug⁵ was administered orally in gradually increasing doses to the 6 children with cerebral palsy previously treated with curare by Denhoff and Bradley¹ with a reasonable degree of success. An accurate comparison of the two drugs in individual patients was thus facilitated. The same general method of determining the optimum dose as that used by Denhoff and Bradley with curare was employed. Only one dose a day was given at first, to avoid any possible cumulative effect. An initial dose of 25 mg per kilogram of body weight was given, and this was increased by successive increments of 5 mg per

kilogram until unfavorable effects occurred. Following this, it was discontinued for several days and then resumed in a lower dosage three times daily for six days. Two of the latter periods were used for therapeutic evaluation—the first in which each dose was half the toxic dose and the second, directly following, in which two thirds the toxic dose was used.

The children studied ranged in age from eight to twelve years. Three presented varying degrees of spasticity alone, 1 had a combination of spastic and athetotic elements, and 2 showed athetotic movements with no spastic components. All were resident patients at the Emma Pendleton Bradley Home during the entire period covered by the observations. Except for the time spent in the performance of specific tests, each child continued his usual daily activities of physiotherapy, academic schooling, occupational therapy and free play throughout the period of study.

CRITERIA FOR EVALUATION

The children were continuously under the daily supervision of the same physiotherapist and trained nurses of the permanent hospital staff, who kept detailed records of the children's activities and reactions. In addition, during the entire experiment, as well as several days preceding and following this period, daily observations and examinations were made. These examinations included the extent of flexion and extension of spastic limbs; the mode and changes in walking and writing; the degree of fullness and length of time that a glass of water could be held; use of pin board, peg ball and tracing board, and more general subjective and objective observations. As a control measure, these same examinations were carried out with the patients receiving curare, curare placebos and no medication.

The electrical threshold for obtaining muscular contractions at four motor points on each patient was also used in an attempt to determine the extent and presence of the curarizing effect. It was realized that this method included the stimulation of some of the muscle fibers directly in addition to the motor itself. However, the more exact method described by Harvey and his associates⁷ was not considered practicable on these children at the time

*From the Emma Pendleton Bradley Home, East Providence, Rhode Island. Formerly resident physician, Emma Pendleton Bradley Home.
¹The quinine methochloride was supplied through the courtesy of E. R. Squibb and Sons, New York City.

Analyses of venous blood to determine the effectiveness of absorption from the gastrointestinal tract and the concentration of quinine methochloride in the blood were done. A modification of the method described by Prudhomme¹⁰ was used. Determinations of the blood pressure, pulse and respiratory rate, as well as complete blood counts and urinalyses, were repeated at frequent intervals before, during and after administration of the drug.

RESULTS

In an effort to obtain definite beneficial effects the dose was gradually increased until undesirable results were elicited in each patient. The dose necessary to cause these varied, in different patients, from 125 to 140 mg. per kilogram of body weight. This amounted to single doses of from 2.5 gm. (37 gr.) to 4.9 gm. (73 gr.), and was less than the 150 to 200 mg. of quinine methochloride per kilogram that Harvey⁶ found to be necessary for oral curarization in cats. Following doses of 80 to 90 mg. per kilogram, blood levels in these patients varied from 4.7 to 23.4 mg. per 100 cc. and averaged 13.8 mg.

On several of the tests and examinations used to evaluate the effects of the drug, an increased relaxation and muscular co-ordination often associated with a decrease in athetotic movements was apparent. However, this was no greater than the frequent variations in the condition of the same children at times when they were receiving curare placebos or no medication. No appreciable change in the electrical stimuli necessary to cause contractions at the motor points was noted.

The unfavorable manifestations in order of frequency were as follows: malaise and a feeling of lethargy and inertia; nausea and vomiting; diarrhea (with repeated daily doses only); and

ringing in the ears. It is interesting that only 1 patient complained of ringing in the ears. This occurred only once, and subsequently when the dose was slowly increased this symptom did not recur. No abnormalities were detected in repeated blood counts, urinalyses or determinations of blood pressure and respiratory rate.

No constant therapeutic effect was noted with quinine methochloride on the 6 children under observation. This was in contrast to the favorable influence of a preparation of curare on the same children.

SUMMARY

Quinine methochloride given orally to 6 children with cerebral palsy in doses that were increased until undesirable results were obtained failed to give a demonstrable curarizing effect. There was no definite evidence that this drug had a beneficial influence on any of the children.

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A RARE TYPE OF ACUTE THROMBOCYTOPENIC PURPURA: WIDESPREAD FORMATION OF PLATELET THROMBI IN CAPILLARIES*

MARR D ALTSCHULE, MD†

BOSTON

IT has long been known that thrombocytopenic purpura is a syndrome occurring in a variety of diseases, such as leukemia and other myelophtic states, aplastic anemia and severe infections, and in reactions to a number of chemical substances. There remains a large group of cases of thrombocytopenia in which careful study reveals no etiologic factor, these are usually called "essential thrombocytopenic purpura." It is probable that this group is not homogeneous. Treatment in patients with acute essential thrombocytopenic purpura is frequently not curative, but spontaneous remissions are common, temporary control of the hemorrhagic manifestations usually follows transfusion, and more lasting relief may occur as a consequence of splenectomy. Accordingly, most physicians exhibit optimism regarding the outcome of the initial attack of purpura in these patients. A patient with essential thrombocytopenic purpura recently died in this clinic, however, the course being rapidly progressive, unimproved by transfusion and otherwise clinically different from that seen in most cases of this disease.

Study of the literature revealed 5 previously reported cases that resembled this one, in all, death occurred after a short illness. In 1936, Baehr, Klemperer and Schiffrin¹ reviewed the data in 4 unusual cases of thrombocytopenic purpura, including one studied by Friedberg and Gross² and another by Gitlow and Goldmark.³ Baehr and his co-workers defined the clinical characteristics and pathological findings common to all these patients and pointed out their resemblance to those of the incompletely studied case reported previously by Moschowitz.⁴

The present case is reported to call attention to this rare type of essential thrombocytopenic purpura. The clinical manifestations of this syndrome are distinctive, and the correct diagnosis may be made ante mortem in the future.

CASE REPORT

A 50 year old Russian born woman (B.H. 58758) entered the hospital complaining of general malaise and abdominal pain of 4 days duration. There was a family history of diabetes, hypertension and rheumatic fever, one

child had died of tuberculosis. The patient had had scarlet fever, measles and pertussis as a child, and for many years had had chronic pelvic inflammatory disease that was treated by means of two operations. The first operation, 6 years before admission, resulted in menopausal symptoms. The second, a hysterectomy, was performed 18 months before admission, at that time, hypertension was noted, but no evidence of anemia. The patient had some what more bleeding during the operation than is usually seen, but transfusion was not considered necessary. She had been careful of her diet for years, but it was within normal limits qualitatively and quantitatively except for some deficiency in fruit juices. The patient was well until approximately 3 weeks before admission, when she began to notice easy fatigability. Four days before admission, generalized aches and pains developed, particularly over the back and about the joints of the extremities. Severe headaches, dizziness and attacks of diffuse abdominal pain associated with vomiting also occurred on that day. The patient vomited approximately a dozen times, the vomitus containing small amounts of bright red blood. On the next day, cough, productive of a small amount of whitish mucoid material streaked with blood, developed, and a severe nosebleed occurred. Spontaneous bowel movements were absent during the 4 days preceding entry to the hospital, but enemas resulted in satisfactory evacuations. On the 3rd and 4th days of the acute illness, arthralgia, headache and malaise persisted, but otherwise the patient felt improved. She was sent to the hospital on the 4th day of her acute illness by Dr. Morris Rutenberg.

Examination was negative except for pallor, petechiae over the legs and face, slight smoothness of the edges of the tongue, old healed abdominal scars, tenderness throughout the abdomen, enlargement of the liver (5 cm below the costal margin), and a spleen that was palpable at the costal margin. The blood pressure was 115/70. Ophthalmoscopic examination was negative.

Sixteen specimens of urine contained small amounts of albumin and a variable number of erythrocytes and leukocytes. The specific gravities ranged between 1.002 and 1.012. Bence Jones protein was not present in the urine. The red-cell count on admission was 1,800,000 with a hemoglobin of 38 per cent (Sahli), and the white-cell count was 13,400 with 80 per cent polymorphonuclear cells, 15 per cent lymphocytes, 4 per cent monocytes and 1 per cent eosinophils. The platelet count was 54,000, the reticulocyte count 22 per cent, the bleeding time over 30 minutes, and the clotting time 2 minutes. The clot retracted poorly. Examination of the stool was negative. The blood nonprotein nitrogen level was 33 mg and the cholesterol level 313 mg per 100 cc, with 142 mg per 100 cc esters, the blood uric acid level was 5.6 mg, and the serum protein level was 6.1 gm per 100 cc, and the icteric index was 10. Gastric analysis revealed no free hydrochloric acid in the fasting specimen and only small amounts in subsequent specimens. The blood Hinton and Kahn reactions were negative. Bone marrow biopsy revealed normal bone marrow. Lumbar puncture on the 7th day revealed normal findings.

*From the Medical Service, 14th Israel Hospital and the Department of Medicine, Harvard Medical School.

†Associate in Medicine, Harvard Medical School, Associate Physician, 14th Israel Hospital.

The patient was given a high-vitamin, high-protein diet, with fluids ad libitum, 100 mg. cevitic acid by mouth daily, and vitamin B complex and cod-liver oil concentrates by mouth. The rectal temperature ranged between 98.6 and 101.0°F. during the first 5 days and then rose progressively to 107°F. on the 9th day, with corresponding changes in the pulse rate. The respiratory rate was not elevated until the 8th day, when it rose to 40 per minute.

Autopsy (1 hour post mortem). The gross findings consisted in generalized pallor, icterus, ecchymoses in the skin of all the extremities, numerous petechiae in the pericardium, endocardium, myocardium, mucosa of the stomach, duodenum, ileum and rectum, and large areas of hemorrhage in the pleuras, bladder wall and both adrenal medullas. The spleen and liver were enlarged, weighing respectively 540 and 2000 gm. The other gross findings

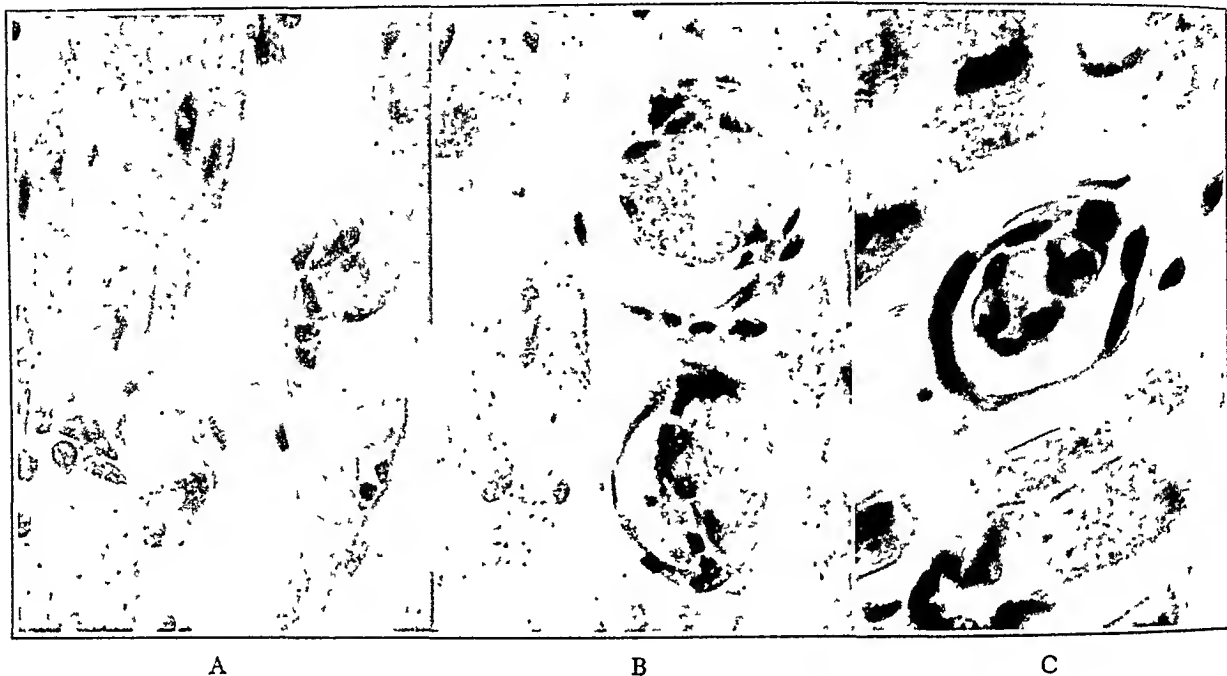


FIGURE 1. *Stages in the Resorption of Platelet Thrombi.*

A—*fresh thrombi*; B—*growth of endothelium over the thrombi*; C—*resorption of the thrombus, with thickening of the capillary wall.*

The patient received 500 cc. of citrated blood on the 3rd, 5th and 8th days after admission, and 1000 cc. of blood on the 7th day, as well as intravenous infusions of physiologic saline and glucose solutions from time to time. The red-cell count never rose above 2,800,000, remaining most of the time between 1,600,000 and 1,900,000, with corresponding hemoglobin levels. The white-cell count varied between 10,000 and 21,000, with a decrease in polymorphonuclear leukocytes, beginning on the 7th day, to between 52 and 58 per cent. The bleeding time was usually more than 30 minutes, decreasing to 11 minutes on only one occasion; the clotting time was always less than 2 minutes. The platelet count decreased progressively to 11,000, and the reticulocytes varied between 7.0 and 12 per cent. Many suppled and small numbers of nucleated erythrocytes were seen. On the 3rd day, the patient became confused, exhibiting mumbling speech and left facial weakness; these signs disappeared completely after a few minutes. Fresh purpuric spots appeared on the face and extremities on that day, and from time to time thereafter. On the 5th day, severe headache developed, and the next day the patient became restless and disoriented as the temperature rose. The icteric index increased to 18. Roentgenograms of the chest revealed findings suggestive of pneumonia, and sulfathiazole was started. The patient rapidly failed, becoming increasingly delirious and somewhat more icteric. She vomited several hundred cubic centimeters of coffee-grounds material, containing clots, on the day of her death.

included congestion of the spleen and of the bronchial and gastric mucosa, edema of the kidneys, slight atheromatous changes in the aorta and several old fibrous bands adherent to the old healed abdominal scars.

Microscopic examination confirmed the gross findings and revealed, in addition, numerous capillary thrombi in the pancreas and heart, a moderate number in the adrenal glands, kidneys and gastrointestinal tract, and a few in the spleen and liver. The thrombi in a few glomerular capillaries also involved the afferent arterioles. Elsewhere, arterioles, venules and larger vessels appeared normal. The capillary thrombi varied from a few platelets adherent to the endothelium to masses of platelets, either recently deposited or else, becoming amorphous and finally shrunken, rather hyaline masses. The capillary endothelium showed evidence of proliferation in these areas, growing over the surface of the masses of platelets; it sometimes remained thickened after resorption of most of the thrombus. There was a minimal leukocytic or fibroblastic reaction in a few areas.

Microscopic examination also revealed acute bronchitis, with early bronchopneumonia, an increase in the number of lymphocytes in the periportal areas in the liver and slight hyalinization of the media of the splenic arterioles.

DISCUSSION

The clinical manifestations in the case reported resemble closely those of the syndrome discussed

by Baehr et al.¹ The disorder, which has been noted only in females, is characterized by rapidly progressive anemia, mild icterus, purpura hemorrhagica and fever. Melena, hematemesis and hematuria may occur; the terminal manifestations consist in stupor, delirium, restlessness and other evidences of intracranial disease. Respiratory infections may precede the appearance of purpura. In addition to anemia, the blood shows leukocytosis, reticulocytosis, the presence in the circulating blood terminally of immature red blood cells, and profound thrombocytopenia. The bleeding time is prolonged, and the tourniquet test is positive; the clotting time is normal, although the clot reacts poorly. Transfusion has no apparent beneficial effect, and death occurs within two weeks to two months after the onset. Splenectomy was performed in 1 of the previously reported cases,¹ and was followed by the death of the patient.

At autopsy, the significant findings consist in normal bone marrow, hemorrhages into the viscera and a large number of thrombotic lesions within the capillaries and, to a lesser extent, the arterioles. Studies made by means of differential stains show these thrombi to consist of masses of platelets, erythrocytes and fibrin are not found in the thrombi. The adjacent endothelium is seen to be proliferating, growing into or over the surface of the thrombi. In some areas, the thrombi are completely covered with endothelium and appear to be shrunken, dense and homogeneous, as if undergoing resorption. It appears that thrombosis occurs in various parts of the body in a succession of attacks. In spite of widespread occurrence of thromboses, there is little or no evidence of parenchymal necrosis.

The rapidly progressive course of the disease, the failure to respond to transfusion, the uniform occurrence of icterus and cerebral manifestations and the specific pathological findings of widespread platelet thrombi are characteristic of this type of thrombocytopenic purpura. Attempts to relate this syndrome to acute disseminated lupus erythematosus because of the purpura and the finding of vascular lesions³ are not valid. The disorder exemplified by the patient in the case reported

above is not characterized by the lymphadenopathy, edema, effusions, signs of pleural and pericardial involvement, specific rash, leukopenia and endocarditis commonly encountered in acute disseminated lupus. Moreover, the vascular lesion is different, consisting in primary alterations in the walls of the blood vessels in lupus, as contrasted to platelet thrombosis in the syndrome of the present discussion.

Baehr et al.¹ suggested that the profound thrombocytopenia seen in this syndrome might be due to withdrawal of enormous numbers of platelets from the circulation; they discussed the possibility that this phenomenon, in a less easily detected form, might occur in other cases of thrombocytopenic purpura. The cause of the damage to the vascular endothelium, which results in deposition of platelets as seen in the syndrome of the present report, is unknown; Schwartzman, Klemperer and Gerber² pointed out the similarity of the vascular lesion in this syndrome to the changes in the blood vessels of animals in which the Schwartzman phenomenon has been induced.

SUMMARY

A case of a rare type of essential thrombocytopenic purpura characterized by the formation of numerous platelet thrombi in the capillaries throughout the body is described.

The syndrome is differentiated from other varieties of essential thrombocytopenic purpura by rapid progression, failure to respond to transfusion and splenectomy and the uniform occurrence of icterus and cerebral manifestations.

330 Brookline Avenue

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MEDICAL PROGRESS

SURGICAL CARE AND OPERATIVE TECHNIC

JOHN D. STEWART, M.D.*

BUFFALO, NEW YORK

NATURALLY enough, the current surgical literature is concerned to a considerable extent with the problems of military medicine, but nevertheless there are contributors who find time for the persistent challenge present in such subjects as hernia, appendicitis and gastrointestinal distention. Evidence is presented favoring the wider applicability of surgical treatment, and one is reminded that it is the physiologic rather than the chronologic age of the patient that matters.¹ As an increasing proportion of the population succeeds in reaching elderly ages, the surgeon is given a chance to show that cancer of the rectum or cancer of the stomach, as examples, can be successfully operated on despite the patient's years.² Furthermore, operative methods are being developed for palliative or curative treatment of hitherto hopeless lesions, such as carcinoma of the esophagus and carcinoma of the pancreas.

WOUND HEALING

What are considered the fundamental principles of the treatment of traumatic wounds are tabulated and discussed by Reid and Carter.³ Hemostasis, débridement, immobilization, avoidance of chemical irritants, preservation of blood supply and maintenance of proper nutrition are among the indisputable points mentioned. Sterilization of fresh traumatic wounds can be only relative, and reliance must be placed on the power of healthy living cells to combat bacteria. Tetanus and gas-bacillus antitoxins are used prophylactically whenever the nature of the wound and the severity of its soiling so indicate. From an experimental study of fresh traumatic and contaminated surgical wounds, Bisgard and Baker⁴ conclude that bactericidal agents applied to wounds do not prevent infection but may cause severe tissue damage and interference with repair. Sulfanilamide, on the other hand, is locally protective and nonirritating. Copious irrigation of the wound with physiologic saline solution is standard practice, but these authors seem to favor mechanical scrubbing of the wound itself while it is being irrigated. In my opinion, such trauma is to be avoided.

The surgeon who prefers to use catgut routinely can find sound instruction based on the physiology of wound healing in an article by Howes.⁵ The complications of wound healing are reduced in number by a decrease in the size of the catgut used, and according to the author no catgut larger than No. 0 need be employed in suturing fascia. Catgut should be used sparingly or not at all in tissues that tolerate catgut poorly, such as the skin, subcutaneous fat, mucous membranes and muscles, but it is overwhelmingly the suture of choice in contaminated wounds. Plain catgut is to be used where rapid healing is to be expected, as in serosal and mucosal surfaces, and in the ligation of all vessels except large arteries, which are not safely sealed off until fibrosis has occurred.

In a rather fantastic communication,⁶ a method is proposed for avoiding exogenous operative contamination completely, based on complete sterilization of the operating room with its contained air and equipment by means of formaldehyde gas. The operating room is hermetically sealed and is entered through four sterile anterooms. Surgeons and patients discard all clothing before entering the sterile rooms and are dressed in sterile overall gowns, which cover the entire body like diving suits. "The patient's skin is cleansed with benzene and then treated for at least ten minutes with a freshly prepared 10 per cent iodine solution, which it is generally unnecessary to remove by means of alcohol." The paper is provocative, and although the methods proposed seem cumbersome to the point of inapplicability, one must admit that it is all too easy to compromise with practical requirements in the matter of surgical asepsis.

Further evidence of the value of vitamin C in wound healing appears in the recent literature as obtained in both clinical and animal research. Patients undergoing operation on the biliary tract in the presence of depleted vitamin C reserves, as shown by the study of the dietary history or determinations of plasma concentrations, are reported to develop a higher incidence of incisional hernia than patients without such depletion.⁷ However, the same authors concluded that, in 12 cases of abdominal-wound disruption, mechanical factors were more frequently to be blamed than vitamin C deficiency. Bartlett, Jones and Ryan^{8,9} report

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, Vol. III, 1942* (Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

*Professor of surgery, University of Buffalo School of Medicine, surgeon-in-chief, Edward J. Meyer Memorial Hospital.

further data from their painstaking investigations in animals and in patients, and Hartzell and Stone¹⁰ submit evidence of similar significance. The latter workers found histologically a failure of collagen production in experimental wounds when vitamin C deficiency was present. Greater than normal tensile strength did not result from an increase in the vitamin C intake above the normal daily requirement, which emphasizes the general conclusion that no benefit is to be expected from an excess of vitamins.

The possible value of vitamin A in wound healing has come under study, but the data do not appear to be decisive. Brandaleone and Popper¹¹ found that wounds made in the abdominal wall of vitamin A deficient rats were epithelialized more rapidly if cod liver oil was applied locally or given orally. Cod liver oil produced no results if vitamin A depletion did not exist. Cod liver oil contains, of course, various substances, some known and some unknown, and the authors offered as control observations the finding that linseed oil applied to the wounds of vitamin A deficient rats did not affect the rate of wound healing.

PROTEIN DEFICIENCY IN SURGICAL PATIENTS

The problem of maintaining nitrogen balance and restoring deficits before and after operation continues to engage the attention that the great importance of the problem deserves. Amino acid mixtures obtained by hydrolytic breakdown of beef, milk and wheat have been used in tube feeding, with satisfactory clinical results.¹² A casein hydrolysate (Amigen), which apparently contains all the essential amino acids, has been given intravenously in several hundred patients with only an occasional mild urticarial reaction.¹³ The authors are convinced that this is the simplest and most convenient way of supplying large amounts of utilizable nitrogen parenterally, and my own experience with infusions of casein hydrolysate leads me to agree. In my studies, the solution has been given at somewhat faster rates without reaction, and with only moderate and transitory elevation of amino acid concentration in the patient's blood. The excretion of amino acids in the urine during and after such infusions appears to be trivial.¹⁴

Brunschwig, Clark and Corbin¹ studied nitrogen balance in a group of 41 patients undergoing a variety of major surgical operations. During the ten days immediately following operation, a nitrogen deficit varying from 3.8 to 175.8 gm was observed in 36 patients. The major factor in the nitrogen loss appeared to be restriction of food intake, although the trauma to tissues at operation and acceleration of metabolism probably contributed. The postoperative nitrogen deficit could be

reduced or even prevented by intravenous infusions of casein hydrolysate. The authors conclude that casein digest and glucose may be employed to maintain and replete nitrogen stores—a conclusion that others have reached before them.

ACUTE APPENDICITIS

Of the various papers on this subject appearing in the past year, several are notable. The exhaustive clinical study of Faxon and Rogers^{15, 17} deserves the attention of the surgeon or internist interested in the acute abdomen. In the clinical appraisal of cases of appendiceal peritonitis, the presence or absence of a mass seemed an advantageous criterion. Of the 671 cases of acute appendiceal peritonitis, in 444 a mass was not present, and the postoperative mortality rate was 15.9 per cent, in the 227 cases with a mass, the rate was 7.1 per cent. The authors state that incision and drainage alone should be done as a primary procedure unless technical removal of the appendix can be readily accomplished, and this principle is especially vital after the fourth day of the disease. Appendectomy should be carried out within six weeks following incision and drainage, as a rule. In the cases without a palpable mass in the right lower quadrant, the highest operative mortality resulted from operation on the fourth or fifth day of the disease. These patients were treated before the use of sulfonamide drugs was introduced in the care of peritoneal infection, and therefore this factor did not enter the study. One of the findings in the survey illustrates the treacherous nature of clinical statistics. The observation was made that appendectomy lasting between fifty and sixty minutes results in about half the mortality rate of either longer or shorter operations. From this, the unimaginative surgeon might conclude that if he found himself getting through the operation before fifty minutes he should find some way of prolonging the procedure to the point of safety.

Guerry and McCutchen¹⁸ discuss the operative handling of the localized appendiceal abscess, as based on extensive personal experience. Mobilization of the head of the cecum, protection of adjacent areas from soiling, proper placing of the omentum and stab wound drainage are among the details recommended. In the illustrations of operative technique, too much gauze seems to be packed into the wound, but the artist may have given a wrong impression.

INGUINAL HERNIORRHAPHY

A number of recent papers on this subject are at hand. In some, the anatomic details are clearly illustrated, a welcome matter to medical students, who realize the shortcomings of the standard text.

books of anatomy in this respect. McVay and Anson¹⁹ discuss what they consider a fundamental error in current methods of inguinal herniorrhaphy, namely, suturing the inguinal layers to Poupart's ligament. They state, "The superior pubic ligament (Cooper's ligament) should be used instead, for it is the normal insertion, it is readily accessible and it is intrinsically strong and directly fixed to bone." After the sac is removed or imbricated as the case may be, the superior pubic ligament is isolated and freed of adjacent preperitoneal connective tissue. The inferior margin of the transversus abdominis aponeurosis and attached transversalis fascia is clarified and sutured to the superior pubic ligament from the pubic tubercle to the femoral vein.

An entirely different approach to the problem is proposed by Jennings, Anson and Wright.²⁰ A low midline suprapubic incision is made down to the peritoneum, and the peritoneum is stripped away from the rectus muscle on the involved side to expose the internal abdominal ring. The hernial sac is either withdrawn or transected at the ring, and the peritoneum proper is usually not entered. Among the advantages of the method are listed avoidance of trauma to the inguinal planes, simplicity of technic, less chance of injuring the ilioinguinal nerve and spermatic cord, and less danger of infection. The authors recognize the limitations of the method, however, and state that it is not applicable to direct or large indirect inguinal hernias, and that major anesthesia and abdominal relaxation are required. The paper is unusually well illustrated.

Clinical and experimental evidence on the use of the buried cutis graft in the repair of hernia is briefly reviewed by Cannaday,²¹ who reports personal experience with the technic. Skin is regarded as better for plastic repair than fascia, on the grounds that skin is "more active," has longer life and is stronger and more resistant to pressure or strain. The author states that cutis may be used in superimposed layers in reconstructing the planes of the abdominal wall. In the experimental studies cited, it was found that the sebaceous glands and hair follicles in the implanted derma disappear early, the sweat glands later. Cannaday apparently has not noted wound infection, such as might come from the bacteria present in the glands and follicles of the buried skin.

CARCINOMA OF HEAD OF PANCREAS

This difficult surgical problem is receiving much study, and definite progress can be reported. Harvey and Oughterson²² have performed local excision of an ampullary growth in 1 case and radical pancreaticoduodenectomy in 5, with 1 fatality.

These authors believe that pessimism is unwarranted and that earlier diagnosis and radical excision of such growths are indicated. Their clinical experience suggests that the external secretions of the pancreas in some patients do not appear to be essential to life. Whipple²³ discusses the reasons for the reluctance hitherto shown by surgeons in tackling carcinoma of the pancreas, and in speaking of technical details points out the great superiority of fine silk over catgut in pancreatic surgery. For carcinoma limited to the papilla of Vater, transduodenal resection, with reimplantation of the common and pancreatic ducts into the duodenum, offers definite advantages in his opinion. Sallick and Garlock²⁴ take a gloomy view and favor routine management of noncalculous obstructive jaundice by external biliary drainage as the initial operative procedure. If the patient survives for more than six months, the lesion is assumed to be benign, and a secondary operation is planned. They state that biliary-intestinal anastomosis at the outset in their series of cases resulted in an operative mortality rate of 48 per cent. Such an attitude appears unjustifiable in view of the palliative results and possible cures being obtained at present in various clinics by bold surgical operation. Attentive preoperative and postoperative care and skill and experience in biliary-tract surgery are undoubtedly requisite in the successful handling of carcinoma of the pancreas.

Fatty infiltration and degeneration of the liver occur not infrequently in carcinoma of the pancreas and the papilla of Vater, and protective preoperative and postoperative measures are analyzed by Schnedorf and Orr.²⁵ The feeding of lecithin, choline, pancreatic extract or lipocaic is recommended as part of the routine management, since the presence of a high concentration of lipid in the liver is associated with impairment of liver function. The authors have hopes that thorough investigation of pancreatic function in patients with vague abdominal complaints may lead to earlier diagnosis of growths in the head of the pancreas or the papilla of Vater. Trimble, Parsons and Sherman²⁶ report another successful one-stage operation for carcinoma of the head of the pancreas. Their patient showed no evidence of interference with the digestion of fat, carbohydrate and protein eleven months after pancreaticoduodenal resection.

A great contribution to the surgical treatment of lesions of the head of the pancreas consists in the report of Ziegler.²⁷ In studying the blood supply of the head of the pancreas in 24 cadavers, he found the gastroduodenal artery to be remarkably constant in its origin, course and distribution, but in 2 cases it gave origin to the middle colic artery. When the gastroduodenal artery does not give

rise to the middle colic artery, preliminary ligation of the gastroduodenal artery and the pancreaticoduodenal artery can be used to render excision of the head of the pancreas and duodenum a relatively bloodless dissection.

SPLENECTOMY

Two suggestions concerning the technic of splenectomy in difficult cases are worthy of mention. When the convex surface of the spleen is densely adherent to the parietal peritoneum, Rives²⁸ advises stripping away the parietal peritoneum along with the spleen instead of trying to separate the adhesions. Singleton²⁹ exposes the splenic artery along the upper border of the pancreas by sectioning the gastocolic ligament. After ligation of the artery, the hilum of the spleen is dealt with in the usual manner, with much less danger of uncontrollable bleeding.

Hamrick and Bush³⁰ report a case of splenosis of the peritoneum and review a part of the literature on the subject. In their case, splenectomy was performed for traumatic rupture of the spleen, and the patient remained well for three and a half years. After death from other causes, autopsy revealed numerous nodules of splenic tissue, up to 4 cm. in diameter, scattered throughout the peritoneal cavity. Microscopically, the tissue was similar to the structure of the adult spleen, with capsule, follicles (without germinal centers) and red pulp containing sinuses filled with red blood cells. This interesting condition is apparently seen only in young persons in whom seeding of the peritoneum with splenic cells has occurred following trauma. No subcutaneous implants have been reported, and no cases have been reported following splenectomy for nontraumatic lesions.

GASEOUS DISTENTION OF GASTROINTESTINAL TRACT

Altmeier and Wadsworth³¹ describe intestinal ileus as a complication of fractured rib and report 10 cases. Irritation of the dorsal sympathetic ganglions and splanchnic nerves appears to be the most plausible explanation, as produced by displacement of the fractured bone, by retropleural edema or hematoma in the paravertebral area or by reflex stimulation of the splanchnic nerves through the peripheral abdominal or thoracic nerves. In 8 of the 10 cases, the fracture was within 5 cm. of the lateral vertebral border. The condition is best treated conservatively without operation if ruptured intra-abdominal viscus can be ruled out.

The free use of nasogastric suction during and after operation is advocated by Singleton, Rogers and Houston.³² The advantages of maintaining

deflation of the gastrointestinal tract through aspiration of swallowed air are summarized, as well as some possible disadvantages of the method. Careful restoration of water and electrolyte lost in this manner is necessary to avoid dehydration and acid base imbalance. Analyses of intestinal gases from dogs with intestinal obstruction are in agreement with the findings of earlier students of the subject, notably McIver, and indicate that most of the gas is swallowed air, since 84 per cent is nitrogen.

Studies of the effects of various drugs on the motility of the human colon are reported by Adler, Atkinson and Ivy.³³ Prostigmine methylsulfate, pituitary extract and ergotamine tartrate were tested with respect to their effect on propulsive motility in the distal colon of 4 patients with colostomies. A combination of the drugs seemed to give better results with less side reaction than a larger dose of the drugs used singly.

DICUMAROL

Experimental and clinical study of the usefulness of 3,3'-methylenebis 4-hydroxy coumarin, or dicumarol, continues.³⁴ This substance causes hemorrhagic sweet clover disease in cattle, and has been isolated, identified and synthesized by Link and his co-workers.³⁵ When 100 to 300 mg is taken orally by the adult patient, retardation of clotting and prolongation of prothrombin time promptly ensue, so far, toxic side actions do not appear to occur. The clotting defect persists for several days, and the only known method of shortening the recovery period is blood transfusion. It seems probable that the drug has clinical applicability in the treatment and prevention of intravascular clotting, thrombophlebitis and pulmonary embolism, as well as in arterial surgery and in sulfonamide therapy of established infection. Preliminary reports suggest that patients may safely be operated on after the clotting mechanism has been inhibited by the drug, although further data are needed.³⁶ In the clinical use of dicumarol, it will probably be necessary to take careful note of individual variation in dosage requirements by frequent measurements of clotting time or prothrombin time, a disadvantage that the method shares with the inhibition of clotting by heparin. The pharmacologic action of the drug remains to be determined, but liver damage is apparently not the basis for its effect.

462 Grider Street

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28391

PRESENTATION OF CASE

A fifteen-year-old schoolgirl was admitted to the hospital because of severe crampy abdominal pain and jaundice.

Seven weeks prior to admission, the patient had a "head cold." This cleared after a week, and she went to the seashore, where she developed a "remarkable tan." Several days later, the scleras were found to be jaundiced.

Five weeks before admission, generalized jaundice developed, unassociated with symptoms other than listlessness and anorexia, and became progressively deeper. A physician treated the patient with a diet limited to fluids. Ten days before entry, she suffered with distention and an attack of severe crampy midabdominal pain, which lasted several hours and was relieved by the passage of flatus and a "diarrhea" stool. Since this episode, attacks of similar pain had become increasingly severe and occurred more frequently. The passage of flatus and loose stools — often ten to twelve times a day — always provided some relief. The attacks bore no relation to meals and frequently awakened the patient from sleep. The stools varied from green to clay but prior to admission seemed to have been most often clay colored. The stools were not tarry and did not contain blood. The urine gradually developed a wine color. A week before entry, when examined at this hospital, the patient was deeply jaundiced. Examination of the heart and lungs was negative. The spleen was felt three fingerbreadths below the costal margin. The temperature was 98°F., and the pulse 100. The patient was advised to remain in bed, take her temperature twice a day, and consume a high-carbohydrate, low-fat diet. Three days later, the patient developed skin ecchymosis on the anterior chest and buttocks. She stated that at this time the attacks of abdominal pain culminated, with some relief in vomiting of copious amounts of fluid. She denied any contact with unusual chemicals or drugs, and there was no evident exposure to rats. During the illness, she gained approximately 17 pounds.

The family history was irrelevant. Four years before entry, an appendectomy was performed be-

cause of "acute appendicitis." Two years later, an abscess of the left kidney was drained, and recovery was complete after two weeks. Catamenia had not appeared for nine weeks.

Physical examination revealed a listless, deeply jaundiced and dehydrated girl who complained bitterly of intermittent attacks of crampy epigastric pain in the left side and across the upper abdomen. The attacks lasted one or two minutes, with a few minutes' interval of relief, and were suggestive of labor pains. Examination of the heart and lungs was not remarkable except for a short systolic murmur audible in the pulmonic area. The abdomen was markedly distended and tympanitic. No masses could be felt because of the degree of distention. There was moderate tenderness over the upper abdomen and to the left of the umbilicus. Dullness was percussed in the right upper quadrant from the fifth rib to three or four fingerbreadths below the costal margin. Peristaltic sounds were diminished in intensity and frequency. There was a slight degree of bilateral ankle edema.

The blood pressure was 140 systolic, 70 diastolic. The temperature was 103.2°F., the pulse 120, and the respirations 30.

Examination of the blood revealed a red-cell count of 4,100,000 with a hemoglobin of 10.5 gm., and a white-cell count of 13,000 with 93 per cent polymorphonuclear neutrophils. The hematocrit was 47 per cent. The urine was the color of port wine and acid in reaction, had a specific gravity of 1.012, showed a +++ test for bile, and contained 5 to 10 white blood cells and 3 to 5 granular casts per high-power field. The stool was semisolid and tan.

The guaiac test was markedly positive, and bile pigment was found to be present. The nonprotein nitrogen was 12 mg. per 100 cc., and the van den Bergh reaction 37.6 mg., direct. The prothrombin time was 75 seconds (normal, 22 seconds). The phosphorus was 2.3 mg. per 100 cc., and the phosphatase 3.3 Bodansky units. A flat plate of the abdomen showed a diffuse haziness. There was no evidence of dilated loops of bowel. In one film, there was a large amount of gas in the stomach.

In spite of supportive treatment in the form of the administration of vitamin B complex, vitamin K, glucose and citrated blood, the patient lapsed into coma and died two days after admission.

DIFFERENTIAL DIAGNOSIS

DR. ALLAN M. BUTLER: Let us briefly enumerate some of the salient features of this history. Seven weeks prior to admission, the patient had

a head cold. Ten days later, she developed jaundice. During the next three and a half weeks of jaundice, there was no fever, pain, vomiting or diarrhea. Five and a half weeks after the onset of jaundice, she suffered from distention, abdominal pain and diarrhea. For a considerable period of the jaundice, there was bile in the stools. The wine-colored urine leads me to assume that there was a mixture of bilirubin, urobilinogen and urobilin in the urine.

When first examined at this hospital six weeks following the onset, the patient was still deeply jaundiced and still had no fever. There was also no bradycardia. The advice to remain in bed and consume a high-carbohydrate, low-fat diet makes one wonder whether the examining physician made the diagnosis of catarrhal jaundice.

DR. TRACY B. MALLORY: The first visit to the hospital was to the Out Patient Department. At that time, the patient was given a house appointment and entered the ward a week later.

DR. BUTLER: I assume that the skin ecchymoses reflected the hypoprothrombinemia of jaundice, which is to be distinguished from vitamin K deficiency. With the former, there is plenty of vitamin K getting in, but in the presence of liver damage it is not convertible to prothrombin.

The absence of fever, I should think, is against Weil's disease. In asking about unusual chemicals or drugs, the physicians were searching for the etiologic factor of the toxic hepatitis.

The distention of the abdomen was, I presume, largely due to ascitic fluid.

One wonders if a hepatitis was not mistaken for appendicitis, or whether with the appendicitis something occurred that caused injury to the liver. We know that colon bacillus infections of the kidney may result in colon bacillus septicemia and consequent hepatitis.

I assume that the pain in the left side and across the upper abdomen had to do with splenic congestion, possibly pancreatitis, gastric dilatation or adhesions about the duodenum. At this point, no mention is made of ascites, but I assume that ascites was present. Apparently, the liver was enlarged, but the edge was not made out, so that we do not know whether it was a smooth edge. No mention is made of any prominent superficial abdominal veins. The serum protein concentration is not reported.

A week after the visit to the Out Patient Department, the temperature rose to 103.2°F. The hemoglobin and cell counts indicate that the patient was not having a hemolytic crisis. The urine contained bile, white cells and granular casts. No mention is made of urobilin or epithelial cells. Bile was present in the stool. The low blood

nonprotein nitrogen probably reflects the high-carbohydrate, low-protein diet and the low blood urea from liver damage. The serum alkaline phosphatase was not elevated as I should have anticipated with this degree of jaundice and liver disease. No blood Hinton or tuberculin reaction is reported.

The facts that x-ray examination showed no evidence of dilated loops of bowel and that the patient was continually having stools indicate no intestinal obstruction.

Do the x-ray films deserve demonstration, and does an x-ray man want to interpret them or do I have to?

DR. MALLORY: I am sorry, but no x-ray man is here.

DR. BUTLER: The films suggest ascites, with diffuse haziness throughout the abdominal cavity, an elevated diaphragm and some congestion at the bases. The heart is pushed up by the elevation of the diaphragm that results from the abdominal distention, which in turn is due to ascites.

If I had been asked to see the patient at this point in her course, I think I should not have said that she had syphilis, actinomycosis, an echinococcal cyst or other parasitic infection or a liver abscess. There was no history of trauma to initiate liver damage. The chances are very much against cholelithiasis, and I do not believe the primary disturbance was related to a cholangitis or that the patient had a portal cirrhosis. Therefore, I conclude that she probably had a toxic hepatitis.

As a pediatrician who does not see a great deal of liver disease in patients of this age, I should have called in a consultant.

I had hoped to be able to call in Dr. C. M. Jones, but unfortunately he is on vacation, so that I cannot benefit by his opinion. From the subsequent course of the patient, it appears that she did not obtain such benefit either.

The best I can do without that consultation is to say that this patient died in cholemia from liver insufficiency due to toxic hepatitis. Since the physical examination suggested an enlarged liver, the pathological diagnosis might well be hypertrophic biliary cirrhosis following a toxic hepatitis, with simultaneous degeneration and regeneration of the liver cells. Or it may be that the degeneration was acute enough to warrant the diagnosis of subacute yellow atrophy.

The etiology, I should think, would remain unknown. We have seen several patients with such a course of disease, and the etiology has been unknown. Strangely enough, Dr. L. K. Diamond at the Children's Hospital has seen three children of one family with a story like this, and the diagnosis was the one that I am making in this case.

I believe that Dr. Jones encountered another family in which several children with similar stories were thought to be suffering from toxic biliary cirrhosis.

I think it will be found that the splenomegaly was of the obstructive type. There may have been some pancreatitis. If there was a portal or splenic thrombosis, it was secondary and did not play a great part in the present course, because portal or splenic thrombosis usually leads to death from repeated esophageal and gastric hemorrhages after a considerable period. If such thrombosis were primary, we ought to have more comment about superficial abdominal veins, collateral circulation and, possibly, esophageal varices. There may have been extrahepatic obstruction of the common duct due to tumor or enlargement of the lymph nodes of the portal fissure. Although nothing was said about epithelial cells in the description of the urine sediment, I should think the kidneys would show cloudy swelling of the tubular epithelium with desquamation of some of the epithelial cells. Because of the past history of draining of a perinephritic abscess, some healed pyelonephritis should be evident at autopsy.

A PHYSICIAN: Is there a possibility of subacute bacterial endocarditis? Were there any blood cultures?

DR. MALLORY: There were no blood cultures. I think this degree of jaundice would be very unusual for bacterial endocarditis.

A PHYSICIAN: Was there a history of pregnancy?

DR. MALLORY: No.

DR. WILLIAM W. BECKMAN: I was bothered by the fact that the spleen was enlarged at the time of the first examination, and I wondered if there were an underlying process, such as splenic thrombosis or cirrhosis.

CLINICAL DIAGNOSIS

Acute yellow atrophy of liver, etiology?

DR. BUTLER'S DIAGNOSIS

Toxic hepatitis.

ANATOMICAL DIAGNOSES

Subacute yellow atrophy of liver

Ascites

Icterus

Peritonitis, chronic fibrous, localized, postoperative.

Operative scar, appendectomy.

Hydrothorax, slight, right.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Dr. Butler has not been present at these exercises very long and, consequently,

does not know the pleasure I take in presenting cases with palpable livers that turn out to be extremely small and atrophic. Of all points in physical examination I think the estimation of the size of the liver is the most unreliable, and totally so in any patient with ascites.

This patient had a liver weighing 1050 gm., which represents a moderate degree of atrophy. It was coarsely nodular, the nodules ranging up to a little more than 1 cm. in size. They were interspersed with deep and rather large depressions in which liver cells are absent. The picture corresponds very closely to what we interpret here as the healed stage of acute atrophy.

One wonders how long the process had been developing. The history was only a little over six weeks in duration, whereas the liver shows considerable fibrosis, rather more than I should suppose could be accounted for merely by condensation of the stroma. The scars are still quite vascular, however, and there are still numerous mononuclear phagocytes, which presumably were attracted by disintegrating liver cells. All active degeneration of liver cells has ceased, and regeneration is still active.

There had also been time for well-marked hypertrophy of the spleen, which weighed 650 gm. The sinusoids are dilated, and the splenic pulp is fibrotic, as one sees in any case with portal hypertension. There were not any readily demonstrable evidences of collateral circulation, however, but esophageal varices are difficult to demonstrate at autopsy even when seen clearly at fluoroscopic examinations during life. I have recently heard of an apparently well-authenticated similar case in which death from a ruptured varix occurred six weeks after the onset of epidemic infectious hepatitis. If this is correct, cirrhosis and portal hypertension must, on occasions, develop with much greater rapidity than we have hitherto supposed. The kidneys, as predicted, show a moderate degree of tubular degeneration consistent with so called "bilonephrosis." There were no other significant findings.

The etiology, as predicted, remains completely mysterious. My inclination is to consider it due to infectious hepatitis,—that is, catarrhal jaundice,—but in the absence of an epidemic I know of no way to prove the point.

A PHYSICIAN: I should like to ask about the nonprotein nitrogen of 12 mg. per 100 cc. That is not a normal figure.

DR. BUTLER: The patient had been living on a low-protein, high carbohydrate diet and had liver disease.

CASE 28392

PRESENTATION OF CASE

A forty-three-year-old man was admitted because of crampy abdominal pain.

Two and a half years before admission, the patient suffered with a gastrointestinal upset, which lasted one day and was characterized by diarrhea, but had no vomiting. Eight months later, he had several attacks of abdominal pain and vomiting, each lasting several weeks. Following each attack, he was quite well. One and a half years before entry, he consulted a physician because of an attack of epigastric distress, which developed after he ate bacon. This attack was characterized by recurrent periods of periumbilical colicky pain, each lasting several hours and somewhat relieved by belching and vomiting. During the attacks, diarrhea developed. However, the stools remained normal in color and did not contain blood or mucus. The physician told the patient that he had a tendency toward ulcer and treated him successfully with a bland diet. Ten days before admission, after a similar attack, he entered a community hospital, where a gastrointestinal barium study was said to have been negative. On the night before admission to this hospital, the gastrointestinal distress recurred and was similar to previous episodes, except that the pain was severer. Obstipation had developed, but no vomiting occurred. During the three months prior to entry, the patient had lost 20 pounds in weight.

The family and past histories were irrelevant.

Physical examination revealed a well-developed, very restless, haggard man who was obviously acutely ill. The skin was dry, and the tongue dry and coated. Examination of the lungs was negative. There were soft apical and basal systolic murmurs. The abdomen was distended, and in the left epigastrium, there was a smooth, nontender mass, which descended with respirations. No edge and no irregularity of the mass could be distinguished. In the left lower quadrant, there was a firm, smooth, movable, baseball-sized mass, which was tender and dull to percussion. There was no abdominal-wall spasm, and no rebound tenderness. Peristalsis was diminished.

Rectal blood pressure was 122 systolic, 88 diastolic. Temperature was 100°F., the pulse 96, and respirations 24.

The blood revealed a hemoglobin (photoelectric-cell technic) and a hematocrit of 14,900. The urine had a specific gravity of 1.025, gave a +++ test for diacetic acid and a + test for sugar, and contained 15 cells per high-power field (a

saline-glucose infusion was administered prior to the collection of this urine specimen). The blood Hinton reaction was negative. A flat plate of the abdomen revealed numerous loops of dilated bowel, particularly of the small bowel. There was some gas in the dilated cecum. The stomach was displaced upward by the dilated loops of bowel. There was a large soft-tissue mass in the left side of the abdomen.

Gastrointestinal decompression was initiated by means of a Miller-Abbott tube. A barium enema was then performed. The barium flowed to the cecum without delay. There seemed to be pressure on the sigmoid by a soft-tissue mass. There was no definite evidence of obstruction in the colon. A large amount of fecal material was present. Numerous loops of dilated small bowel were visible.

Operation was performed on the second day after admission.

DIFFERENTIAL DIAGNOSIS

DR. HORACE K. SOWLES: In this patient with a history of somewhat less than two years of real trouble, the attacks suggest to me mechanical interference with the small bowel. Probably, mechanical interference with the biliary tract or gall bladder can be excluded. The reference of pain to the periumbilical area is characteristic of small-bowel lesions. Its colicky character and the fact that the patient was quite well between attacks are typical of transient, partial obstruction. The diarrhea, I think, can be explained by the fact that this pain stimulated peristaltic action. I do not believe the obstruction was ever complete. The most recent attack was somewhat severer, and for the first time, obstipation was noted. It is rather curious that no vomiting occurred with that attack, because with interference of small-bowel action, nausea and vomiting are quite prompt.

The patient had a weight loss of 20 pounds. That undoubtedly is significant and suggests, of course, that the lesion was a neoplasm.

The family history is irrelevant.

On physical examination, the mass first described as being in the epigastrium was smooth and nontender, no edge and no irregularity being demonstrated, which means that they did not believe it was the spleen. I suppose it might have been a cyst of the pancreas or omentum. Against a cyst of the pancreas is the fact that later physical and x-ray examinations placed the tumor mass lower in the abdomen, pressing on the sigmoid. This perhaps rules out cyst of the pancreas but does not rule out cyst of the omentum.

The blood pressure was not significant. The pulse was somewhat rapid at the time of admis-

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sion to the hospital, showing an acutely ill man, and was perhaps a reaction to pain and discomfort. The hemoglobin was low, again perhaps suggestive of a neoplasm. The hemoglobin probably was not lowered by blood loss because we have no story of blood loss in the bowel movements. The white-cell count was 14,900, which is somewhat elevated. If the patient had an ulcerative lesion of the small bowel, with associated infection, that might account for it. The x-ray films are not particularly helpful. There were dilated loops of bowel and some gas in the dilated cecum, and the stomach was displaced upward—a picture of partial obstruction. The colon and cecum filled without delay. There was no evidence of lesions in the cecum, but there was extrinsic pressure on the cecum by a soft-tissue mass.

What was the soft-tissue mass that we assume to have been the cause of the trouble? I suppose that it might have been a cyst of the omentum, perhaps a tumor of small bowel. If so, it probably was not carcinoma, which gives a small cicatricial lesion as a rule, causing partial obstruction, and does not attain the size described in this case. Lymphosarcoma would be more likely to attain this size, and there might be more than one lesion and tumor of the small bowel itself causing intermittent obstruction; the soft-tissue mass described on x-ray study might be retroperitoneal lymphoma. I do not believe we need assume that there were multiple tumors, however. The symptoms were probably due to mechanical interference with the bowel by tumor. It might have been a cyst, possibly of the kidney, more likely of the omentum, and still more probably a tumor—a lymphoma or lymphosarcoma of the small bowel.

Perhaps Dr. Schatzki can give more information than appears in the written description.

DR. RICHARD SCHATZKI: The flat abdominal film shows the markedly dilated loops of small intestine described in the record. The cecum is moderately distended. I cannot see if the rest of the colon is distended. The soft-tissue mass is indefinite on the flat film; I cannot be sure of it. A

barium enema, however, shows it very clearly as displacing the sigmoid downward, without affecting the cecum. There is one region in the proximal transverse colon that, on the postevacuation films, looks a little narrow. I cannot imagine that the examiner would have missed a lesion of that size during fluoroscopy. I think the appearance is due to the enormous amount of fecal material that the patient had in his colon.

CLINICAL DIAGNOSIS

Intussusception?

DR. SOWLES'S DIAGNOSIS

Lymphosarcoma of small intestine.

ANATOMICAL DIAGNOSES

Polyp of ileum.

Intussusception.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was explored. No definite preoperative diagnosis was recorded, although a note in the record at least suggested the possibility of recurring intussusception as the cause of the symptoms. At operation, a large sausage-shaped mass of small bowel, 75 cm. long, was found, which was an obvious intussusception. An attempt to reduce it proved impossible. It was necessary to resect the entire area, about 180 cm., as it turned out, of small bowel. At the head of the intussuscepting mass was an area where the mucosa of the ileum was markedly swollen, edematous and, at one point, frankly polypoid. There can be little doubt that intestinal polyps had been present for a considerable time, at least the two and a half years that the history covers, and had repeatedly acted as the focus behind which intussusception developed. On each of the earlier occasions, spontaneous reduction must have occurred.

DR. SCHATZKI: I looked carefully for intussusception in the flat film. Usually one can see some evidence of it. There was none, however.

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MASSACHUSETTS MEDICAL SERVICE

LITERATURE concerning Massachusetts Medical Service — the Blue Shield — was mailed last Tuesday night to every licensed physician in Massachusetts. This included copies of the "Application of and Agreement with Participating Physicians" and the "Schedule of Surgical, Obstetrical and X-Ray Benefits."

Since many people in Massachusetts are anxiously waiting to participate in the plan and since the majority of industrial leaders are eager to provide their employees with an inexpensive and effective method of budgeting for unexpected surgical expense, all means to expedite actual operation of the Blue Shield should be provided. Furthermore,

medical societies in other states are watching with interest the development of this medical-service plan, which is still another example of Yankee foresightedness, cohesiveness and altruistic enterprise.

The mailing of contracts and fee schedules, scheduled for August, was retarded by the tremendous amount of detail necessary to make the plan operable. Because of this delay and because of the unsettled conditions prevailing in the Nation, all physicians are urged to sign both copies of the "Application and Agreement" and to return them immediately.

Further delay in the Blue Shield plan will lessen public interest and encourage the proponents of government-controlled medicine. The more rapidly Blue Shield begins to protect the health of Massachusetts wage earners, the sooner this very important health problem plaguing the mind of a war-conscious community will be solved. In view of the urgent need for an adequate scheme for the provision of medical care, let it never be said that the physicians of Massachusetts offered "too little — too late."

SALVATION ARMY APPEAL

THE Greater Boston Annual Maintenance Appeal of the Salvation Army will begin on September 28. More than two thousand volunteer workers will assist in the collection of \$250,000, the goal for 1942-1943. The twenty-seven cities that comprise the Metropolitan Division will be included in the drive.

At the opening dinner, to be held at the Boston Chamber of Commerce on September 29, the *Carrier Salvation* will be launched; the sister of an aviation ordnance man who died in action at Pearl Harbor has been selected as sponsor of the campaign ship. Governor Saltonstall, Mayor Tobin, naval, army and labor leaders and others will join in the launching.

The objective for this year, which is \$50,000 more than the goal in 1941, can be attained only through the greatest generosity on the part of those who contribute. The Salvation Army, which has done so much for the needy, must

raise its quota if it is to function in the difficult days ahead, when it may have to meet even greater demands for help because of shortages of fuel and other vital necessities.

The need is great, and there are few worthier causes. The appeal should inspire every public spirited citizen to do his utmost. Physicians, who have responded generously in former campaigns, are urged to continue to lead their communities in making the work of the Salvation Army possible.

MEDICAL EPONYM

ARGYLL ROBERTSON PUPIL

Although he credits Stellwag von Carion with the statement that tabes dorsalis and spinal paralysis may cause paralytic myosis, the account of the rigid pupil in his report, entitled "On an Interesting Series of Eye symptoms in a Case of Spinal Disease, with Remarks on the Action of Belladonna on the Iris, etc.," in the *Edinburgh Medical Journal* (14:696-708, 1869), together with a later report, "Four Cases of Spinal Myosis; with Remarks on the Action of Light on the Pupil," in the same journal (15:487-493, 1869), has served to affix permanently the name of Douglas Argyll Robertson (1837-1908), lecturer on diseases of the eye at the University of Edinburgh, to this phenomenon. The following quotation is from the earlier article:

On examining the eyes, I found both pupils contracted to little more than pin points, the right rather the smaller of the two. I could not observe any contraction of either pupil under the influence of light, but, on accommodating the eyes for a near object, both pupils contracted.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

CASE HISTORY DEATH FOLLOWING PARTIAL SEPARATION OF THE PLACENTA AND VAGINAL DELIVERY

A twenty-four-year-old Polish woman began to bleed when approximately eighteen weeks in her second pregnancy, and continued to do so off and on until she was sent to the hospital in the thirtieth week. The past history was irrelevant, the only operative procedure being a cesarean section, which terminated her first pregnancy. After

the initial bleeding mentioned above, the patient was in bed the greater part of the time and was seen frequently from then on. The blood pressure and the urine remained normal; no vaginal examination was made. In spite of the frequent recurrences of moderate bleeding, the patient was not hospitalized until about the thirtieth week, when the bleeding became freer. No vaginal examination was made on entry, but five days later, labor started spontaneously. When it had progressed to the point where the cervix was dilated two fingerbreadths, there was so much free bleeding that delivery was attempted. It was a breech presentation, and a footling extraction was accomplished, apparently without difficulty. The patient, however, went immediately into shock and, despite transfusion, died half an hour after delivery.

Comment Undoubtedly, this patient was carried along from the eighteenth week for the purpose of obtaining a live child. In view of the previous cesarean section and the fact that the pregnancy, when labor started spontaneously, had reached the point of possible viability, it is strange that cesarean section was not immediately performed. Had it been done, this patient would not have died of hemorrhage. It is interesting that the death certificate stated the cause of death to be "placenta previa," but the details given by the visiting physician indicated that the bleeding came from a partially separated placenta. It is quite likely that if, as the record stated, delivery was attempted when the cervix was dilated but two fingerbreadths, this death was due to hemorrhage, possibly associated with rupture of the lower segment.

The handling of this patient from the beginning, although conscientious, was unintelligent, the method of delivery ill advised, and the death avoidable.

WAR ACTIVITIES

PROCUREMENT AND ASSIGNMENT SERVICE

The following release from Services of Supply, Office of the Surgeon General, has recently been forwarded to all corps area and state chairmen by the Procurement and Assignment Service.

The Surgeon General of the Army published detailed information concerning policies governing the initial appointment of physicians as medical officers on April 23, 1942. Necessary changes are given wide publicity, at his request, in order that the individual applicants, and all concerned in the procurement of medical officers, may know the status of such appointments.

The current military program provides for a definite number of position vacancies in the different grades. The number of such positions must necessarily determine the promotion of officers already on duty and, in addition, the appointment of new officers from civilian life. Such appointments are limited to qualified physicians required to fill the position vacancies for which no equally well-qualified medical officers are available. Such positions calling for an increase in grade should be filled by promotion of those already in the service, in so far as possible, and not by new appointments.

If this policy is not followed, it would definitely penalize a large number of well-qualified lieutenants and captains already on duty by blocking their promotions, which have been earned by hard work. In view of these facts, it has been deemed necessary to raise the standards of training and experience for appointment in grades above that of first lieutenant.

With this in view, the Surgeon General has announced the following policy, which will govern action to be taken on all applications after September 15, 1942:

All appointments will be recommended in the grade of first lieutenant with the following exceptions:

Captain. 1. Eligible applicants between the ages of thirty-seven and forty-five will be considered for appointment in the grade of captain by reason of their age and general unclassified medical training and experience.

2. Below the age of thirty-seven and *above* the age of thirty-two, *consideration* for appointment in the grade of captain will be given to applicants who meet all the following minimum requirements:

- a. Graduation from an approved medical school.
- b. Internship of not less than one year, preferably of the rotating type.
- c. Special training consisting of three years' residency in a recognized specialty.
- d. An additional period of not less than two years of study or practice limited to the specialty or both.

3. Eligible applicants who previously held commissions in the grade of captain in the Medical Corps (Regular Army, National Guard of the United States or Officers Reserve Corps) *may be considered* for appointment in that grade provided they have not passed the age of forty-five years.

Major. 1. Eligible applicants between the ages of thirty-seven and fifty-five *may be considered* for appointment under the following conditions:

- a. Graduation from an approved school.
- b. Internship of not less than one year, preferably of the rotating type.
- c. Special training consisting of three years' residency in a recognized specialty.
- d. An additional period of not less than seven years of study or practice limited to the specialty or both.
- e. The existence of appropriate position vacancies.
- f. Additional training of a special nature of value to the military service, in lieu of the above.

2. Applicants previously commissioned as majors in the Medical Corps (Regular Army, National Guard of the United States or Officers Reserve Corps) whose training and experience qualify them for appropriate

assignments *may be considered* for appointment in the grade of major provided they have not passed the age of fifty-five.

Lieutenant Colonel and Colonel. In view of the small number of assignment vacancies for individuals of such grade, and the large number of reserve officers of these grades who are being called to duty, such appointments will be limited. Wherever possible, promotion of qualified officers on duty will be utilized to fill the position vacancies.

Much misunderstanding has arisen concerning recognition by specialty Boards and membership in specialty groups. It will be noted that mention is not made of these in the preceding paragraphs. This is due to the variation in requirements of the different boards and organizations. Membership and recognition are definite factors in determining the professional background of the individual, but are *not* the deciding factors, as so many physicians have been led to believe.

The action of the Grading Board, established by the Surgeon General in his office, is final in tendering initial appointments. Proper consideration must be given such factors as age, position vacancies, the functions of command and original assignments. All questionable initial grades are decided by this board. Due to the lack of time, no reconsideration can be given.

There are in the age group from twenty-four to forty-five more than a sufficient number of eligible, qualified physicians to meet the requirements of the Medical Department. It is upon this age group that the Congress has imposed a definite obligation of military service through the medium of the Selective Service Act. The physicians in this group are ones needed *now* for active duty. The requirements are immediate and imperative. Applicants beyond forty-five years may be considered for appointment only if they possess special qualifications for assignment to positions appropriate to the grade of major or above.

MISCELLANY

TUBERCULOSIS AND INDUSTRY

Industrial health and tuberculosis in industry are topics of great concern to all nations at war. Britain, the senior partner of the United Nations by length of service, was confronted much earlier than we were by problems arising from the conversion of peace economy to war production. The following are abstracts from recent British publications.

INDUSTRIAL HEALTH

(Newman, G. *Britain Today* February, 1942.)

The recent reformation in the health and life of the industrial worker in Britain is one of the most impressive and remarkable chapters in the progress of preventive medicine. It records a development from disorder, neglect and confusion to regularity and discipline, and from arbitrary mismanagement to scientific planning. It has become physiologic, social and personal in objective. This is of national importance, for it affects five or six million men and women workers in the factories, and twenty million workers outside them. It sets a standard for all employment, and crystallizes British conceptions and traditions. It is perhaps the most popular of all public methods

of preventive medicine, and has in it the elements of a liberal education. It improves and fortifies the health of the workman,—his only capital,—increasing his dividend, lengthening his life and enlarging his opportunity and personality. It affects the whole man—his habits and character, his domestic life, his family and his home, as well as his workplace. It is a great school of citizenship and health education of body, mind and spirit.

The worker himself and not his factory environment is the vital factor. His fitness, capacity, endurance and willpower are the chief requirements in the prevention of the overstrain, fatigue and disharmony that may be the precursors of disease. This is the center of gravity.

SOME REFLECTIONS ON THE TUBERCULOUS IN INDUSTRY

(Mann, B. *Tubercle* 23 72-75, 1942)

For years, the aftercare attention meted out to post sanatorium cases has been the Cinderella of the Tuberculosis Service. This has been due to a variety of factors. In the main, the results were less spectacular than those of the operating theater and hence never achieved the same popularity in the lay mind, and again with a floating peace-time unemployed population of about three million, healthy labor was at a premium.

Information about tuberculous disease or previous treatment at a sanatorium or dispensary should be made compulsory for all persons entering industry. This is the practice of military boards, and there appears no legitimate reason why this should not be incorporated into the civilian industrial life of the country. Such a measure would ensure the control of infection in the interests of the health of the community. Naturally such a course will occasion opposition. It will be argued that this represents an encroachment on the freedom of the individual. However, freedom would be an intolerable institution if it permitted a man indiscriminately to infect his fellow creatures with disease.

An extremely strong case can be made out in view of the recent extension of the defense orders making the treatment of scabies compulsory in the interests of national health. The extension of such a defense regulation to incorporate tuberculosis should prove a relatively simple legal measure.

MISS RADIOSCOPY IN FACTORIES

(Hall, A. S. *Lancet* 1 161, 1942)

Much has been written lately concerning the value of mass radiography of the chest, and reports, among others of investigations into the pulmonary disease of Australian recruits, British sailors and University College Hospital students are available but so far little has been done in this country with the ordinary unselected civilian population. Anyone who has wished to conduct such an examination must at once have become conscious of the many difficulties, of which lack of suitable apparatus and the reluctance of the population to submit to examination are the chief. Nevertheless, few doubt that these difficulties will soon be overcome.

X-ray screening of the chest was offered to the work people in two factories, the management allowing this to be done in working hours. In the first, 60 per cent and in the second, 97 per cent came for examination. Of 575 people examined in the first factory, 3 were found to be tuberculous. Of 792 examined at the second factory, 2 were known to have phthisis and 2 others were found to have active disease.

WEEDING OUT TUBERCLE

(Editorial *Lancet* 1 357, 1942)

Commenting on the above article by Dr A. Stephen Hall, a later issue of the *Lancet* states in an editorial:

In each factory about 0.5 per cent of the workers had clinically significant tuberculosis. This percentage is lower than that found in similar mass surveys elsewhere, a common figure being between one and two per cent. The question therefore arises whether the examiner sees as much and as truly on the fluorescent screen as on the developed film.

In this welter of instrumental aid when employers and employees alike have been led to expect surveys which will wipe out tuberculosis it may be well to add a cautionary word. No diagnosis is ever made on a fluorogram; any doubtful or abnormal finding calls first for a full size radiogram and, should the abnormality be confirmed, a thorough physical overhaul. If the whole method is not to be discredited, and if hard ships and misery from faulty diagnoses are to be eliminated, as much thought must be given to the training of personnel as to the choice of apparatus.

If a worker submits voluntarily to examination he will naturally ask that he and his family are not to suffer financially while undergoing treatment for what, in his opinion might have healed at work. Tuberculosis is coming to be regarded more and more as a disease of economics.—Reprinted from *Tuberculosis Abstracts*, September, 1942.

CORRESPONDENCE

HUNTINGTON TUMOR CLINIC

To the Editor. The following letter has been sent to all physicians who have, in the past, recommended patients to the Huntington Memorial Hospital. I am sure that its publication in the *Journal* will give additional publicity to the new arrangement.

NATHANIEL W. Faxon, M.D., Director
Massachusetts General Hospital
Boston

* * *

MASSACHUSETTS GENERAL HOSPITAL AND THE HUNTINGTON TUMOR CLINIC

The clinics formerly conducted at the Huntington Memorial Hospital have been transferred to the Massachusetts General Hospital. Records of former patients have also been transferred and are available. Letters have been written to many of the former patients telling them of the change and giving them new appointments. Notices informing physicians of the change have already been published in the *New England Journal of Medicine*.

The work is being carried on by former members of the staff of the Huntington Hospital, who are also on the staff of this hospital.

It has been the policy of the Huntington Hospital to care for patients of the small income and medium income groups. This same policy will be continued. The Massachusetts General Hospital has long conducted a tumor clinic and the Huntington clinics will be merged with the Tumor Clinic.

The Tumor Clinic will be divided, hereafter, into the Morning Clinic and the Afternoon Clinic. Former Huntington patients will be assigned to the appropriate cor-

sponding clinic. Morning patients will enter through the Out Patient Department. Afternoon patients will be admitted directly to the Tumor Clinic through the Main Entrance, White Building.

New patients to either clinic should be recommended for admission by their physicians. Free patients or those who can pay only the usual small outpatient fee should be referred to the Morning Clinic. Patients who can pay a nominal sum (in excess of the usual outpatient fee) should be referred to the Afternoon Clinic.

Physicians must clearly state whether patients are referred for

Diagnosis or Consultation. In such cases, the patients will be returned to the physician with a following letter giving results and recommendations.

Diagnosis and Treatment. In such cases, diagnosis will be made in the Tumor Clinic and treatment will be carried out in the appropriate hospital department. When treatment is completed, patients may be returned for interval care to their physicians.

The organization of the Tumor Clinic is founded on the policy of having the clinic conducted as a joint project of the General Surgical Department and Radiological Department, assisted by consultants from the recognized medical and surgical specialties. Following this policy, the General Surgical Clinic and Radiological Clinic will be conducted daily, both morning and afternoon, but patients having lesions coming within the province of the various specialties should be sent on the following designated days:

Morning Out-Patient Clinic (9:30 a.m.)

Monday — Lymphoma and leukemia
Tuesday —
Wednesday — Urological and neurological
Thursday — Laryngological
Friday — Dermatological
Saturday — Gynecological

Afternoon Semi-Private Clinic

The General Surgical Clinic and Radiological Clinic will receive patients daily at 2 p.m., except Saturdays, when the clinics will be held at 9:30 a.m.

Patients for whom consultation in the various specialties is necessary should come the afternoon of the day that the appropriate specialty is cared for in the Morning Clinic, except that all gynecologic patients should come on Saturday morning.

NATHANIEL W. FAXON, M.D., *Director*

REPORTS OF MEETINGS

WILLIAM HARVEY MEDICAL SOCIETY

A regular meeting of the William Harvey Medical Society of Tufts College Medical School was held at the Beth Israel Hospital on May 8. Dr. Richard B. Cattell, of the Lahey Clinic, discussed "Cancer of the Colon and Rectum."

A consideration of some of the important fundamental anatomic and physiologic factors operating in this region aids an analysis of the subject. The right colonic contents are fluid and are teeming with bacteria, in contrast to the semisolid, relatively clean contents of the left colon. Certain difficulties are encountered because of the characteristics of the region. The bowel is thin walled, and this

makes anastomosis more difficult. The blood supply is from vessels that are essentially end arteries with few collateral vessels. The mobility of the colon decreases as the anus is approached, and the danger of injuring blood vessels and nerves in mobilizing the lower segments is thus increased. The lymphatic supply, which influences the kind and speed of spread of cancer, is much richer on the right than on the left side of the colon.

To realize the importance of this subject, one has but to know that 25 per cent of all cancer occurs in the gastrointestinal tract and that half of this is in the colon and rectum. It is twelve times as frequent in this region as inflammatory lesions. Sixty per cent of the malignant lesions occur in the rectum. Fifty-six per cent of the rectal lesions are in males, and 61 per cent of colonic lesions in females, the over-all distribution being about equal in the two sexes. The age incidence is about ten years older in cancer of the colon, in which 44 per cent of cases occur between sixty and eighty years of age. However, 16 per cent of the entire group studied at the Lahey Clinic were under forty years of age.

The pathogenesis of cancer in this region is better understood in many respects than that of cancer in the stomach. In the rectum, the presence of pre-existing polyps is of recognized significance. This condition may have a hereditary tendency, and congenital adenomatous polyposis is known to be a definitely precancerous condition. Polyps are found in about 2 per cent of the general population.

The commonest early symptoms of rectal carcinoma are bleeding, discomfort, tenesmus and change of bowel habits; those of the colon are bleeding, mucus, change of bowel habits, anemia, weight loss and vague abdominal complaints. Symptoms should never be attributed to the more benign of two possibilities in this region. The fallacy of this practice is borne out by the statistics, which reveal that 15 per cent of the patients proved to have rectal cancer had had operations for hemorrhoids within six months, and that another 15 per cent with the same diagnosis were treated medically. Change of bowel habits is present in 80 per cent of all patients with large-bowel cancers, but abnormal stools decrease from 86 per cent in rectal cases to 9 per cent in those with lesions in the right colon, whereas pain increases in exactly inverse proportion. Diagnosis should be made from the history, abdominal and rectal examinations, proctoscopy and sigmoidoscopy, barium and double contrast enemas, biopsy and exploratory laparotomy. The history is often irrelevant, but rectal lesions are within reach of the examining finger in 50 per cent of cases.

The preoperative care of such patients requires several days, and is divided into the restoration of the local and general physiology to as near normal as possible. Locally, the fecal material is completely removed by the most gentle method, and the bowel is kept clean. Generally, the patients are in sore need of fluids, vitamins and, possibly, transfusion. Cleansing of the bowel is best performed in one procedure and colonic irrigations are then carried out up to the day of operation. In cases of obstruction, the Miller-Abbott tube may be used to decompress the small bowel, but is only a temporary expedient and must be supplemented by operation within twenty-four to forty-eight hours to decompress the large bowel.

The technic of the operation for cancer of the large bowel is largely a matter of choice and experience of the surgeon. Surgery is the only sure way of curing such lesions. The operability of a lesion depends on early and accurate diagnosis, the extent of the lesion, the type of the operation and the experience of the surgeon. At the

Lahey Clinic, the Mikulicz obstructive resection is usually carried out for colonic lesions. In the rectum, where the sigmoid must always be sacrificed because its blood supply is embarrassed by the removal of the drainage areas from the rectum, either a one stage Miles or a two stage Lahey resection is carried out. During the last fifteen years, the operability has increased from 47 to 89 per cent, but the mortality has been reduced from 36 to 7 per cent. Thus although more borderline cases come to operation, improved preoperative care and operative technique have markedly decreased the mortality.

The prognosis of large bowel cancer is variable. If colonic lesions are confined to the bowel, there are 90 per cent five year cures, but this drops to 50 per cent when the regional lymph nodes are involved. When the lesion is removable, the curability is 45 to 50 per cent. The total salvage is 33 per cent but many patients who are operated on are greatly benefited. In the Mikulicz operations on the colon, the mortality is less than 3 per cent whereas Mikulicz operations on the whole have a 12 per cent mortality. This is at least partly explained by the better mobility of the colon, which allows for more radical excision of the malignant growth. It was pointed out that although 60 per cent of the patients with cancer of the right colon have enlarged regional lymph nodes many of these may be inflammatory. This may be favorable for the prognosis but should not influence one's judgment of the amount of mesentery to be removed.

BOSTON CITY HOSPITAL

The third of the series of lectures sponsored by the Boston City Hospital House Officers Association was held at the hospital on May 12. Dr Edward D. Churchill discussed "The Problems of Wartime Thoracic Surgery."

Most traumatic chest wounds do comparatively well if hemorrhage is not rapidly fatal and if there is not undue tampering with the wound at the first-aid stations. Since it is impractical, if not impossible to assemble a competent thoracic team in the combat area, only a minimal amount of actual surgery is carried out there. First aid is aimed at the arrest of hemorrhage from the wound, the physical correction of the disturbed cardiorespiratory physiology and the prevention of infection.

The second of these is by far the most essential in chest wounds and is peculiar to this region. In the so-called sucking wounds, a large defect of the thoracic wall causes an open pneumothorax and mediastinal flutter. These factors result in cardiac as well as respiratory embarrassment, and large wounds of this type are rapidly fatal if uncorrected. Small wounds, even of both sides, are compatible with life. Treatment of such wounds is aimed at closing the defect as thoroughly and quickly as possible by any means. Skin flaps, if available, may be sutured, or some such substance as cellophane may be employed. Above all, the pleural cavity should not be packed with gauze, for this is unnecessary for the restoration of physiology and the gauze is poorly tolerated. One of the sulfonamides in the wound before closure is desirable.

The second important problem concerns tension pneumothorax or the accumulation of air under pressure in the pleural cavity. This may occur in the previously mentioned large wall defects after closure if there is injury to a bronchus, or if a penetrating wound allows escape of air from a bronchus. In either event, air enters the pleural space at each expiration and is stored under increasing pressure, with resultant respiratory embarrassment. Such patients are cyanotic and have characteristic

grunting respirations. Subcutaneous emphysema is a common complication, but needs no specific emergency treatment if the underlying pleural tension is properly handled. This merely requires the making of a hole in the chest wall with whatever means is available. Preferably, a trocar and small catheter connected to a water-sealed trap should be used. Another complication, which demands immediate therapy, however, is the backflow of interstitial air around the bronchi to cause mediastinal emphysema. The first indication of its presence is seen in the suprasternal notch. Its presence disturbs particularly the return of blood to the heart by compressing the great veins, and there is subsequent decreased cardiac output and shock. The treatment of this serious emergency is the performance of mediastinotomy through a cellular thyroid incision. This starts like a low tracheotomy except that, instead of opening the trachea, a finger is inserted beneath the sternum.

The third serious problem results from multiple fractured ribs. Crushing injuries not infrequently cause fractures anteriorly and posteriorly, with a mobile fragment between. The same effect is found in bilateral fractured ribs. In either event, there is paradoxical movement of this mobile fragment, with subsequent respiratory embarrassment proportional to the amount of displacement of the fragment. This is a difficult condition to treat, especially since respirators—the ideal thing—certainly will not be available in field hospitals. Strapping often makes the pain and disability worse, but may be tried temporarily. Relief is sometimes afforded if the patient lies on the affected side. Traction may be improvised by the use of such things as skin towels on the ribs and the consequent steadying of the fragment.

Finally, there is the question of slowly progressive hemorrhage, such as that occurring in a lacerated lung. Bleeding from major vessels is usually rapidly fatal. Since the pleural cavities can contain as much as 5000 cc of fluid it is obvious that fatal hemorrhage may occur before there are any signs of mechanical interference with respiration. Therefore, the degree of hemorrhage should be judged by the usual criteria employed in general. Treatment is not standardized. The blood may be aspirated, and an equal amount of artificial pneumothorax may be substituted in an attempt to allow the bleeding point to seal itself by putting the lung at rest. The use of such aspirated blood for autotransfusion is impractical, and may even be dangerous in war wounds, in which contamination is frequent. If nothing is done at the time, there may be 1000 to 1500 cc of blood in the pleural cavity, augmented by an additional amount of serous exudate from the trauma. This may demand aspiration to relieve respiratory distress and if so air should be reinjected to prevent further hemorrhage. If the amount is small, nothing need be done. If the accumulation is going to be removed at a later date, it should be carried out gradually or with the substitution of air. Because the thick blood may create a mechanical problem for aspiration, a trocar and catheter (Nu 24 to 26) may be used. This should be left in place for only four to six hours, however, and should not be left as a drain. In general, an uninfected hematoma of this region should not be drained in the ordinary sense. Since the very presence of hemithorax is sufficient cause for a moderate fever and a minimal leukocytosis, a microscopic or cultural examination of the material removed is necessary to establish the diagnosis of sepsis. Despite older theories, it is now considered feasible in low grade infections with no constant source of organisms from the lung or chest wall to carry out pri-

mary closure aided by the use of the sulfonamide compounds locally and systemically.

The definitive treatment of chest wounds will be successful and can be carried out only where there are experienced anesthetists. A general surgeon can do a good piece of work with the help of a good intratracheal anesthesia; a competent anesthetist can accomplish this with inadequate equipment, whereas the inexperienced man is never certain even with the best equipment. In injuries of the lung, the patient should be kept somewhat dehydrated to prevent pulmonary edema, and in hemoptysis, the use of blood or blood-substitute transfusions is postponed as long as possible.

Dr. Churchill discussed the types of drainage and their indications. Open drainage, or rib resection, allows free entrance of air. This is used only when there is an encapsulated accumulation of pus and when there are firm adhesions between the rest of the lung and the pleura. Constant close drainage, or an intercostal tube, allows the escape of fluid and air but not the entrance of air. Some form of valve, preferably a water-sealed valve, is employed. This is used to relieve a continuing pressure pneumothorax, and should be used only rarely in a rapidly increasing infectious exudate. Intermittent closed drainage is similar, except that the tube is clamped and only periodically aspirated. It may be used occasionally postoperatively or when there is no way of arranging an escape valve. It may also be employed for forty-eight hours following extensive débridement to guard against tension pneumothorax and to give warning of hemorrhage or sepsis; if there is no septic exudate at that time, it is removed. But many surgeons prefer primary closure when the patient is not under constant personal observation, for otherwise the tube may be left too long or mishandled. One must rely on somebody en route to insert a tube if necessary, and the sulfonamides must be used to make the procedure safe.

Empyema was too common an occurrence during World War I. Before any therapy is carried out, a careful diagnostic thoracentesis is done. If foul pus is obtained, there is only one course—immediate open drainage. If such pus is not encountered, cultures are made, and treatment is decided on accordingly. In the early stages of acute spreading pleuritis, the process is a cellulitis, just as in early cases of peritonitis. In such cases, drainage is more harmful than advantageous, especially in the chest, where there is the additional danger of pneumothorax. Only when an abscess has formed should drainage be carried out, and then by rib resection at the dependent spot. The commonest mistakes are for the diagnostic thoracentesis to be made too low and the rib resection too high.

Retained foreign bodies in the lung or pleura should not occasion any immediate worry. They are best left alone unless thoracotomy and débridement are necessary. Smooth metal bodies seldom cause subsequent trouble, but jagged shell fragments not uncommonly lead to suppuration.

BOOK REVIEWS

Foundation for a Science of Personality. By Andras Angyal, M.D., Ph.D. 8°, cloth, 398 pp. New York: The Commonwealth Fund, 1941. \$2.25.

This book is a profound study of personality. The author is a philosopher as well as a physician. He attempts to show that the psychology of personality can be a science, although it is not yet one. Dr. Angyal goes

back to the beginning and borrows much from Aristotle. He applies Aristotelian attitudes to new phenomena in the field of psychiatry. How well he carries out this in his book must be determined by the individual reader.

This is a very complicated and thoughtful volume that most readers will find slow going. Before it could be useful to the clinician, it would have to be thoughtfully digested and reinterpreted. It will never be a book for the general reader, but will be interesting to the educated physician who likes occasionally to think.

Cerebrospinal Fever. By Denis Brinton, D.M. (Oxon), F.R.C.P. (Lond.). 8°, cloth, 163 pp. Baltimore: Williams and Wilkins Company, 1941. \$3.00.

Few serious diseases have been more affected by chemotherapy with the sulfonamide group of drugs than cerebrospinal fever. The mortality of 50 per cent in World War I has been reduced to 10 per cent in the present conflict. With a few pills, patients with a dangerous and fatal disease are now usually well in a week or less. Rules of dosage are needed, and complications of treatment must be avoided; serum therapy and repeated lumbar puncture, however, are considered obsolescent. This excellent monograph, timely in its appearance, gives a physician all that he needs to know about one of the miracles of modern medicine. The book should be in every Army and Navy hospital and in the hands of every physician called on to treat cerebrospinal fever. Each section of the subject is clearly stated, and the book contains an adequate list of references and an index. The few illustrations show the complicating rash.

Workmen's Compensation and the Physician: A manual for the use of general practitioners and insurance carriers. By Henry H. Jordan, M.D. With a discussion of traumatic neuroses by Paul H. Hoch, M.D. 8°, cloth, 180 pp. London: Oxford University Press, 1941. \$3.00.

The general practitioners and representatives of insurance carriers do not always see eye to eye, regarding the importance of rendering certain medical services to an injured employee. This difference of opinion causes them to waste valuable time in litigation and keeps the industrial-accident boards busy. These conflicts do not add to either the comfort or the well-being of the injured employee. To remedy this situation, Dr. Jordan, equipped with an eighteen years' experience in workmen's compensation and in his capacity as a referee in orthopedic and traumatic surgery, wrote the present manual. Since impartiality seems to have been his guide in the treatment of every phase of this subject, this book is likely to bring about a better understanding, on the part of all concerned in workmen's compensation, of their common problems.

The treatment of disabilities arising "out of and in the course of employment" is discussed from all angles. Is there a "causal relation" between the confirmed incident during the employment and the pathologic condition causing the disability? Could the sequence of events leading to the accident directly or indirectly have produced the pathologic changes or at least influenced to a major degree a pre-existing major condition? Is there any unintentional exaggeration or malingering or distortion of the true picture, willfully carried on to obtain greater remuneration? What is the most effective method of treatment—a matter of great concern to patient and doctor alike? (Here, paradoxical as it may seem, the author points out that the more expert physical-therapy measures or costly orthopedic

appliances, properly handled, not only prove a blessing to the patient but in the long run constitute a great financial saving to the insurance carrier in the settlement of the claims, and to this end, brief but fairly complete chapters are devoted to the physical therapy and the orthopedic appliances. Is the disability partial or complete? Is it temporary or permanent? What will it mean to the patient in terms of ability or inability to engage in gainful occupation? All these questions and many more are answered by the author, a competent man, who has reviewed some thirty thousand cases of workmen's compensation and has developed a keen sense of values and fair judgment.

This book is a distinct addition to a rather meager collection of works on an important subject.

The 1941 Year Book of Public Health Edited by J. C. Geiger, M.D., D.P.H. 12°, cloth, 544 pp., with 20 illustrations. Chicago: The Year Book Publishers, Incorporated, 1941. \$3.00

The purpose of these publications is being slightly missed. The year book idea is excellent, and thus one is well written, but its purposes and values might profitably be restudied. It is inevitable that a book written for physicians, administrators, hospital and school authorities, public health nurses and others should contain much material that physicians alone are not interested in and that they should not be led to buy or read unless they can feel assured that they are being brought really up to date in their own spheres of activity and responsibility.

The reviewer is disturbed by the omission of what seems to him vital material relating to the period covered. For example, rheumatic fever is given ten pages, but the chemoprophylaxis of rheumatic recurrences is not mentioned. In the reviewer's opinion, the most promising contribution of the decade has thus been overlooked. In the field of child nutrition, it is not necessary to be told again that the child of today is the man of tomorrow when instead one might be reminded that a simple method of plotting physical fitness from two to twenty years of age has at last been devised. Both these subjects were presented and editorially commented on in the *Journal of the American Medical Association*, so that their omission will be noted by physicians who keep themselves informed those who do not keep themselves informed will be more entertained than instructed by buying and reading the book.

The physician needs a year book in the field of disease prevention, but it need not be so voluminous as this and should be much more comprehensive. As for the others, —administrators, hospital and school authorities and public-health nurses,—the reviewer will not presume to speak, he hopes that they will not be discouraged by his own disappointment.

An X-Ray Atlas of Silicosis By Arthur J. Amor, M.D. (London), M.Sc. (Wales). With translation of the legends into French by Robert E. Horne, M.A., and a foreword by Sir Wilson Jameson, M.D. (Aberdeen), F.R.C.P. 4°, cloth, 206 pp., with 72 plates. Baltimore: The Williams and Wilkins Company, 1941. \$8.00

This atlas of silicosis consists mainly of reproductions of x-ray films depicting the various stages of silicosis, silicosis as found in various industries and complications of silicosis, as well as films for differential diagnosis. There are five short chapters dealing with the nature of silica dust and the pathology of silicosis, a short discussion on

the radiologic examination of the lungs and the clinical manifestations, and a few remarks on the prognosis.

Unfortunately, the author discusses silicosis in various industries, such as iron ore mining, slate quarrying and pottery, giving the impression that the films are characteristic for the industry. The statement is made under slate quarrying that calcification at the hilum is almost specific to that industry. This statement can hardly be justified in view of the many variable factors that play a part in this disease, such as infection, personal resistance and the degree of tuberculosis that may complicate the picture.

The descriptive material is fairly adequate, although many statements are rather dogmatic and lack clarity. Thus, the author states that in many obvious cases of pulmonary tuberculosis, tubercle bacilli are not found in the sputum, but he fails to state whether or not culture growths and guinea pig inoculations of the sputum were included. In this country, Dr. Pinner and his associates have shown that tubercle bacilli can be demonstrated in over 90 per cent of clinical tuberculosis and that a negative sputum in the presence of pulmonary disease is significant provided culture or guinea pig inoculations have been included. Much confusion still exists in the minds of many physicians about when early silicosis begins and the exaggerated lung markings of the normal chest ends. At best, the question of silicotuberculosis, or tuberculosis without silicosis, is still subject to individual interpretation.

The atlas, nevertheless, is a welcome addition to the growing literature on silicosis. The book should be of value to the roentgenologists and especially to the physician interested in the ever increasing and complicated problems of silicosis.

A Manual of the Treatment of Fractures By John A. Caldwell, M.D. 8°, cloth, 150 pp., with 76 illustrations. Springfield, Illinois: Charles C. Thomas, 1941. \$3.50

This manual, written primarily for medical students, house officers and general practitioners, fills a distinct need for a concise description of the accepted methods of treating the usual types of fractures. Many excellent and exhaustive books have been written about fractures, but no small compendium has as yet given the essentials of treatment so clearly and briefly. The book is illustrated with good line drawings, and each chapter is supplemented by a number of references to medical literature for those who wish further information.

The Furtherance of Medical Research By Alan Gregg, M.D. 8°, cloth, 129 pp. New Haven: Yale University Press, 1941. \$2.00

Few can be so well qualified to discuss the furtherance of medical research as Dr. Alan Gregg, director for the medical sciences at the Rockefeller Foundation. The author will have the hearty support of all thinking people in his belief that the growth, indeed the survival, of interest and support for medical research depends on widespread understanding of what it is and what it is worth. He further argues with commendable vigor that in democracies the public attitude toward research plays a major role in making truth useful. The lectures that compose this book were given at Yale University under the Dwight Harrington Terry Foundation. The first lecture is entitled *Medical Research Described*, the second, *Universities and Foundations*, and the third, *The Medical Research Worker*. At the end of the book,

Appendix I concerns an outline docket item, and Appendix II is an outline for presenting a proposal for a capital grant for building an institute. The book is delightfully written and interspersed with witticisms and appropriate historical references. It is the reviewer's opinion that this book should be read by every medical student and that all librarians should draw special attention to it for study, not only by students but by faculty members.

Maude Abbott: A memoir. By H. E. MacDermot, M.D., F.R.C.P. (Can.). 8°, cloth, 264 pp., with 10 illustrations and 1 portrait. Toronto: The Macmillan Company of Canada, Limited, 1941. \$2.50.

Maude Abbott's list of interests and accomplishments is in itself enough to place her in the forefront of women who have become physicians. She was a pioneer in education for women and their training in medicine. A great contributor to medical museums and a frequent stimulator of historical research in others, as well as a distinguished contributor to the history of medicine in Canada, she is of course noted mostly for her extensive work on congenital heart disease; but, as has been pointed out, in addition to her efforts in this field, her most important contribution was the vital stimulus given to others by a spirit that was indefatigable. Few persons have set a more rapid pace than Maude Abbott, and memories of her are always associated with the tremendous pressure of activity and an abundance of work at hand. She seemed never to relax and even at the age of seventy was actively engaged in research. She applied for a fellowship with the Guggenheim Foundation in anticipation of an elaborate revision of her abstracted cases of congenital heart disease when she had already passed the age of three score years and ten.

Dr. MacDermot has written an excellent biography of one of the most unusual and stimulating persons in recent medicine. Maude Abbott stands out as a beacon, the greatest woman physician of Canada and one of the outstanding physicians in her generation. The biography is intimate, stimulating, well written and finely documented. In it, one finds an inspiration second only to that which could be given by the subject herself. To have known Maude Abbott was a privilege given to many during her long career. To those who knew her and to the many thousands of physicians and students who will follow, this biography will be welcome.

A Text-Book of Neuro-Anatomy. By Albert Kuntz, Ph.D., M.D. Third edition, thoroughly revised. 8°, cloth, 518 pp., with 307 illustrations. Philadelphia: Lea and Febiger, 1942. \$6.00.

This standard book has long made a name for itself in the field of neurologic literature. A few changes have been made in this new edition, but the general form has not been altered.

A Textbook of Surgery. By American authors. Edited by Frederick Christopher, M.D. Third edition, completely revised and reset. 4°, cloth, 1764 pp., with 1538 illustrations. Philadelphia and London: W. B. Saunders Company, 1942. \$10.00.

This single-volume text on surgery has become, since 1936, when the first edition was published, the standard reference book of its type in America. More than just a student's book, this is a work for surgeons, written by men of wider clinical experience and leaders in progress.

The third edition contains new material on war injuries and sections on the applications of the sulfonamide

group of drugs. The book is, indeed, as the editor marks in his new preface, "an up-to-date, practical treatise on surgery."

Association for Research in Nervous and Mental Diseases. Volume XXI. The Diseases of the Basal Ganglia. Proceedings of the Association, December 20 and 21, 1941. New York City. 8°, cloth, 719 pp., with 268 illustrations and 15 tables. Baltimore: The Williams and Wilkins Company, 1942. \$10.00.

Nineteen chapters, by various authors, deal with the anatomy, physiology and clinical aspects of diseases associated with the basal ganglia of the brain. Much of the book is highly technical, particularly the sections on anatomy. This part is authoritative and up-to-date. The clinical chapters are of less value, although the drug treatment of paralysis agitans is well handled. The value of surgical treatment of disease of the basal ganglia is still uncertain. The last few chapters emphasize this uncertainty.

The book is well edited and handsomely published. It forms the twenty-first volume of the publications of the Association for Research in Nervous and Mental Diseases.

A Manual of Pharmacology, with Its Applications to Therapeutics and Toxicology. By Torald Sollmann, M.D. Sixth edition, entirely reset. 4°, cloth, 1298 pp. Philadelphia: W. B. Saunders Company, 1942. \$8.75.

This new edition, the sixth, of a standard work, first published in 1917, is somewhat disappointing. Errors have crept in, the current literature is not always carefully surveyed, and the book has lost something of the authoritative character associated with the older editions. It is still useful, but the reader is warned to beware of reference citations without personal verification.

Communicable Disease Nursing. By Theresa I. Lynch, R.N., Ed.D. 8°, cloth, 678 pp., with 156 illustrations and 5 color plates. St. Louis: The C. V. Mosby Company, 1942. \$3.75.

This is a carefully written, exhaustive manual of detailed instructions in the technic of elementary nursing procedure. It should serve as a valuable textbook for nurses who are being trained in the care of patients with communicable disease.

Chinese Lessons to Western Medicine: A contribution to geographical medicine from the clinics of Peiping Union Medical College. By I. Snapper. With a foreword by George R. Minot, M.D. 8°, cloth, 380 pp., with 132 illustrations. New York: Interscience Publishers, Incorporated, 1941. \$5.50.

It is always a welcome privilege to make ward walks with a distinguished clinician. This book transplants the reader to the wards of the Peiping Union Medical College Hospital. The author has been recognized as a clinician with an erudition born of intensive study at the bedside and a wide knowledge of the literature.

The diseases indigenous to the locale are taken up. Primary among these are the various avitaminoses, tuberculosis, which is quite rampant, infectious diseases, such as kala-azar, and acute opium poisoning, to mention but a few of the widely diversified group of subjects.

In view of present world conditions, this volume should prove particularly valuable to those who may find themselves intimately associated with our ally.

(Notices on page x)

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CESAREAN SECTION IN MASSACHUSETTS IN 1941

ROBERT L. DENORMANDIE, M.D.

BOSTON

THIS report is the fifth of the five-year study of cesarean sections sponsored by the Massachusetts Department of Public Health and the section of Obstetrics and Gynecology of the Massachusetts Medical Society.

The usual questionnaires were sent to one hundred and sixty-four maternity hospitals, and replies were received from all.

* * *

In Massachusetts in 1941, there were 71,234 live births and 1796 stillbirths, a total of 73,030. Of these, 63,266 were reported to us as having occurred in hospitals. Two thousand four hundred and thirty-six cesarean sections were performed. One abdominal pregnancy is not included in the statistics. There were 14 hysterotomies, making a total of 2450 abdominal deliveries.

The incidence in 1937 was 1:30.3, in 1938, 1:28.7, in 1939, 1:32.2, in 1940, 1:29.2, and in 1941, 1:29.8.

Little comment is necessary regarding Table 1, except that the number of extraperitoneal operations and of Porro operations increased, being respectively 44 and 41. Six elective and 25 emergency Waters operations were performed. Three patients died in the emergency group; these are commented on below. Of the other types of extraperitoneal operations, 3 were elective and 10 emergency; none of these patients died. All the emergency operations followed long, ineffectual labors. Some of these patients were undoubtedly neglected, but others were under competent supervision of well-trained physicians all the time, and why they were allowed to remain in labor as long as they were is difficult to understand. In at least several of these cases, sulfanilamide was used in the abdominal cavity, and the patients recovered. In the extraperitoneal group, 3 sections were done following failure of operative attempts by vagina. In 1 case, the patient was in labor for twenty-four hours and was trans-

fused four times, and the wound became septic and drained for thirty-seven days. The baby was stillborn and hydrocephalic.

Of the Porro operations, 14 were done for fibroid uterus, 5 because of ruptured uterus, 4 following

TABLE 1. *Summary of Abdominal Deliveries.*

OPERATION	NO OF CASES
Cesarean section	2436
Emergency	1126
Elective	1309
Not reported	1
Type of operation	
Low	1336
Classical	1009
Waters or extraperitoneal	44
Porro	41
Not reported	6
In labor	806
Not in labor	1601
Not reported	29
Membranes ruptured	387
Membranes unruptured	2014
Not reported	35
Hysterotomy	14
Total	2450

separated placenta in cases in which the uterus failed to contract, and 3 following failure of operative attempts at delivery from below. In 6 cases, the uterus was atonic, and hysterectomy was performed to save the patient. The remaining 9 cases were done for various other indications.

As shown in Table 2, there were 14 hysterotomies—6 for cardiac disease and 7 for nephritis or

TABLE 2. *Indications for Hysterotomy.*

INDICATION	NO OF CASES
Cardiac disease	6
Nephritis	6
Hypertension	1
Severe bleeding	1
Total	14

marked hypertension. The final case was reported as one of severe bleeding, no other cause being given. The reason for operation is not clear.

In Table 3, which lists the types of anesthesia used, the great increase in the use of spinal anesthesia is interesting. Nitrous oxide, oxygen and

TABLE 3. *Types of Anesthesia.*

ANESTHETIC	No. of Cases
Nitrous oxide, oxygen and ether	1244
Ether	272
Cyclopropane	166
Spinal	641
Nitrous oxide and oxygen	8
Local	62
Other	30
Not reported	13
Total	2436

ether is still the first choice, and the use of cyclopropane has dropped.

Table 4 shows the reported indications for operations in which the baby died. As in previous years, the greatest number of babies were lost from placenta previa and separated placenta. It should be noted that 18 babies were lost following previous sections. The reason for these deaths in almost all cases was that the operation was done because the patient went into labor or ruptured her membranes at about the seventh month. Some of the babies,

TABLE 4. *Indications for Operation in Cases with Death of the Baby.*

INDICATION	EMERGENCY CESAREAN SECTION	ELECTIVE CESAREAN SECTION
Placenta previa	49	2
Separated placenta	48	—
Previous cesarean section	10	18
Toxemia	6	10
Disproportion	10	5
Prolonged or inefficient labor	6	—
Obstructing tumor (fibroids)	3	1
Failure of operative attempts	3	—
Malposition	2	1
Fetal distress	2	—
Previous suspension	2	—
Ruptured uterus	2	—
Previous dead baby	—	2
Cardiac disease	1	1
Diabetes	1	—
Tuberculosis	—	1
Eclampsia	1	—
Prolapsed uterus	1	—
Prolapsed cord	1	—
Spastic uterus	1	—
Hydramnios	1	—
Previous third-degree tear	—	1
Labial varices	—	1
Postmaturity	—	1
Surgical emergency	1	—
Bizarre	—	1
Not reported	—	4
Totals	151	49

however, were full term, and it is difficult to explain why they were lost, although one must always realize that even in delivery by vagina a certain number of infants die. It is to be expected that many of the babies in emergency sections die because of hard labor or for other good reasons that can hardly be blamed on the operation. But the loss of so many babies in elective sections raises the question whether the technic was satisfactory

or whether the operations were done at the proper time in the gestation.

Table 5 presents the detailed indications for cesarean section. The same comment is made on this group of cases that has been made in the other reports.

In many cases of placenta previa, the patient could have been delivered exactly as well if not better by vagina, and it is hard to believe that the

TABLE 5. *Indications for Cesarean Section.*

INDICATION	No. of Cases
Previous section	722
Contracted pelvis and disproportion	491
Placenta previa	237
Separated placenta	106
Toxemia	114
Eclampsia	8
Malposition of baby	109
Breech	88
Transverse	15
Face	4
Shoulder	1
Oblique	1
Dystocia	247
Dystocia	34
Labor without progress	38
Test of labor	110
Cervical dystocia	46
Uterine inertia	18
Contraction ring	1
Previous surgical operation	50
Repair of perineum	22
Amputation of cervix	12
Previous uterine operation	15
Previous rectal operation	1
Associated medical condition	45
Cardiac disease	17
Tuberculosis	4
Diabetes	16
Chronic nephritis	4
Friedrich's ataxia	1
Blood dyscrasia	1
Ankylosed hip	2
Previous obstetric disaster	76
Elderly primipara	58
Obstructing tumor (fibroids)	44
Fetal distress	11
Prolapsed cord	7
Following operative attempt	10
By request or for sterilization	10
Ruptured uterus	6
Spontaneous	2
Previous section	4
Bicornate uterus	7
Postmaturity	8
Malformation of fetus	1
Fractured pelvis	1
Surgical emergency	1
Labial varix	1
Prolapse of uterus	1
Congenital dislocation of femur	5
Twins	1
Error in diagnosis	19
Bizarre	39
Not reported	2436
Total	2436

indications "contracted pelvis" and "disproportion" were valid when the babies were found to weigh only 5 or 6 pounds. This happened in too many cases. One cannot help believing that it seemed to the operator the easiest way to terminate a slow labor.

There were 8 cases of eclampsia, with 4 deaths. Again, it is obvious that the prenatal care of these women was inadequate. Whether it was the fault of the patient or of the doctor in charge, there is no way to determine, but the loss of 50 per cent of the cases is surely a very poor result.

Few comments are necessary on the remaining indications. In this, as in previous reports, the indication "following operative attempts" has had to be recorded. Criticism must again be made of surgeons who perform a cesarean section simply at the request of the patient or for purposes of sterilization, without any other adequate reason.

It is interesting that in a case of spontaneous rupture of the uterus, the patient had had in a previous pregnancy an inverted uterus for which a Spinelli operation was done. She went through this pregnancy satisfactorily until near term, when the uterus ruptured in the line of the old Spinelli incision. She was immediately operated on and recovered.

In 5 cases, the recorded indication was "twins." This does not mean that these were the only cases of twins, but in these cases no other indication was given. It is doubtful if these operations were in any way necessary. It should also be noted that in 1 case a large baby was suspected, no x-ray film was taken, a cesarean section was done, and twins were delivered.

Every year, there are a number of cases for bizarre indications on which there seems no need for further comment.

Table 6 presents a summary of the 52 cases in which maternal death occurred, a mortality rate of 2.1 per cent. As in previous years, emergency operations accounted for the greatest number of deaths. The fact that elective operations resulted

in previous years, the division has been nearly equal.

Of the 3 Porro operations resulting in death, all were done because of bleeding, and 2 were complicated by the presence of placenta accreta. Two of these deaths are classified as due to hemorrhage, and 1 is assigned to sepsis.

The three Waters operations in the group of maternal deaths were done after long labors with ruptured membranes. One death is assigned to

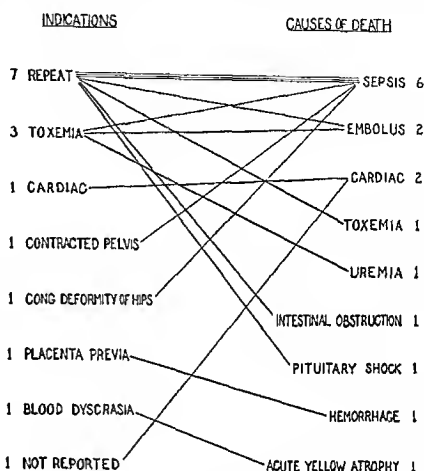


FIGURE 1. Maternal Deaths in 16 Elective Cesarean Sections.

pulmonary edema, 1 to hemorrhage, and 1 to sepsis. The patient who died from hemorrhage was transfused eight times.

Figures 1 and 2 present the indications for operation and the causes of death in the elective and the emergency cesarean sections, respectively.

Of the 16 deaths following elective sections, 6 were from sepsis. Criticism must again be directed at the surgeons who lost these 6 cases. Of the 3 toxemic cases, 1 patient died of an embolus and the other 2 might well be classified under the toxemias, but in 1 of these the patient failed to excrete any urine and the physician regarded the cause of death as uremia.

The patient who died from intestinal obstruction had a large hernia as the result of a previous cesarean operation. The present operation was performed without complications. During convalescence, there was some vomiting, and a Levine tube was used without relief. The vomiting became worse. Apparently, a pneumonia developed

TABLE 6. Summary of Cases with Maternal Death

DATA	NO. OF CASES
Emergency operation	36
Elective operation	16
Type of operation	
Low	16
Classical	30
Porro	3
Waters	3
In labor	20
Not in labor	32
Membranes ruptured	13
Membranes unruptured	39
Babies	
Living	40
Dead	12

in the death of 16 patients shows that cesarean section is not always a safe procedure. In these 52 cases, 40 babies lived, and 12 were lost. In 1941, the deaths following classical sections were far more numerous than those after the low type of opera-

in the right base, and the patient died without relief of the intestinal obstruction. Autopsy showed that there was incarceration of loops of the small intestines resulting from the old hernia. It seems from the facts presented in the questionnaire that this case was not handled intelligently.

The death from hemorrhage occurred in a patient with placenta previa who had had nine previous normal deliveries and who had been in the hospital for fifty days, spotting occasionally.

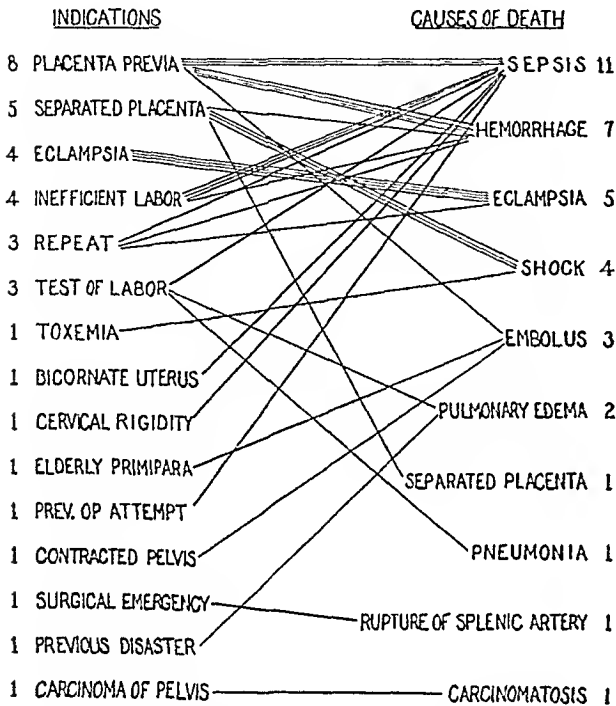


FIGURE 2. Maternal Deaths in 36 Emergency Cesarean Sections.

Operation was finally decided on, and an elective section was done. The patient went into shock and died of hemorrhage. It seems hardly reasonable to have delayed operation for fifty days with more or less spotting occurring all the time. This surely must be regarded as a preventable death.

The case in which the indication is "not reported" is the only case of death in the five-year study on which we have been unable to secure an intelligent, complete report. Repeated efforts to obtain the facts in this case have been unsuccessful. The questionnaire was returned with the statement that it was an elective section and that the cause of death was "acute cardiac dilatation precipitated by vasomotor collapse." No comment on this diagnosis is necessary.

The patient with blood dyscrasia had an unusual blood picture, bleeding from the mucous

membranes and vomiting a large amount of blood. In spite of all treatment, she steadily failed.

Of the 36 deaths that followed emergency sections, sepsis again was responsible for the greatest number. One case in this group that warrants examination had as an indication "cervical rigidity." This patient, a forty-year-old primigravida, was said to be two weeks overdue, and for this reason, an attempt at induction of labor was made. Castor oil and pituitary extract were given in small doses, but the attempt was unsuccessful. Two days later, the membranes were ruptured manually, and a Voorhees bag was introduced with considerable difficulty. It was stated that the cervix was hard to dilate, and that the bag promptly came out. The patient had only indefinite labor, and following a consultation a cesarean section was decided on. A low transverse section was done. At the time of operation, the temperature was 99.6°F. The following day, it rose to 101°F., and climbed steadily until death occurred from sepsis on the eighth postoperative day. This appears to be a typical case of meddlesome midwifery. There was obviously no indication to induce labor, for the patient was perfectly well and the cervix was not favorable for induction. The only reason given was that she was two weeks beyond her calculated date. On failure of medical induction, mechanical induction was attempted. It was obvious when the Voorhees bag was expelled so quickly that the surgeon had not placed it within the uterus. This case is a tragic illustration of the fact that so long as physicians attempt to induce labor without the ability to judge whether or not the patient is ready for induction, bad results are inevitable. It is cases such as this that keep the death rate higher than necessary.

Two deaths, those with indications "surgical emergency" and "carcinoma of the pelvis," cannot be attributed to obstetric complications.

* * *

The results obtained in the cesarean sections in 1941 were excellent, as they were during the entire five-year study. However, they could and should have been better, for it is obvious that many of the deaths were preventable. Far too many deaths are still occurring from sepsis. There is obviously altogether too much haphazard operating. This situation can be improved only by careful study of each case and the mapping out of as definite a procedure as possible for its management. As has been said repeatedly in these reports, cesarean section is an easy way out of a difficulty, but too often has fatal results.

CARCINOMA OF THE BRONCHUS*

GEORGE W HOLMES, MD†

BOSTON

THIS presentation is based on a review of the recent literature, a study of the 158 proved cases treated at this hospital and reported by King,¹ Churchill² and Adams and Davenport,⁴ and an examination of the records of 68 additional cases seen from November 1, 1940, to March 1, 1942, inclusive. The latter group was selected for more intensive study because it was made up of patients who were seen during a period when the methods of diagnosis and treatment were better understood and when supervoltage x-rays were available for the treatment of nonsurgical cases.

Since early, correct diagnosis is of paramount importance and since the number of patients reaching the surgeon at a time when surgical cure is possible is very small, I have limited this discussion largely to the roentgenologic findings in the early stages of the disease and to its treatment with the roentgen rays.

GENERAL CONSIDERATIONS

Cancer of the bronchus is not a rare disease, occurring about as often as cancer of the rectum. The present operative mortality is not formidable, being approximately that of cancer of the stomach. Five year surgical cures have been obtained in 4 to 6 per cent of cases. In this series, there were no five year cures by irradiation although several cases are reported in the literature, however, this method of treatment offers much in the way of relief of symptoms and in some cases of definite prolongation of life.

The progress of the disease is usually rapid, its duration from the date of the first symptom to death being a matter of months rather than years. For this reason, early diagnosis and prompt treatment are imperative, the delay of a month before institution of treatment may mean the difference between success and failure. It is a disease of men (rarely of women), usually in the so called 'cancer age'. The early symptoms and signs are not characteristic and may be entirely absent. The late symptoms are those of its complications, and when they occur the disease is, as a rule, incurable.

Roentgenologic examination often gives the first clue to a correct diagnosis and should be so conducted that all possible information is obtained.

The responsibility of the roentgenologist in these cases is great. The diagnosis is established by bronchoscopy, thoracoscopy or surgical exploration, and these procedures should not be delayed when the clinical and roentgenologic findings suggest early bronchial cancer. The type of tumor, as determined from a specimen taken at bronchoscopy, is of great consequence in the decision of what form of treatment should be undertaken. Oat cell and undifferentiated carcinomas are radio sensitive tumors and usually disappear locally under this form of treatment, whereas the surgical results in the same groups have been uniformly bad. Adenomas and the slower growing types of malignant tumors are radioresistant, but often show excellent results when treated surgically. Consequently, a biopsy should be obtained when ever possible. Advanced cases with lung necrosis or empyema are probably made worse by intensive irradiation and should be treated surgically, if at all.

STATISTICAL DATA

In the 68 cases observed since November, 1940, histologic classification was as follows: epidermoid carcinoma, 26 cases, adenocarcinoma, 4 cases, oat cell carcinoma, 8 cases, undifferentiated carcinoma, 6 cases, unclassified, 14 cases, and without biopsy 10 cases. At the end of March, 1942, 45 of the 68 patients were known to be dead, 8 were living, and 15 could not be traced. Ten of the entire group were considered favorable for surgical treatment. Of these, 3 were living when last heard from, but their present status is unknown. During the same period, 47 patients were selected for irradiation. Of these, 8 were living on April 1, 1942, 2 were free from evidence of disease, 4 were symptomatically improved, and 2 were in the terminal stage of the disease. The remaining 11 patients received no special treatment. The average duration of life for the 45 patients known to be dead, from the time diagnosis was established until death, whether they received special treatment or not, was four and a half months. For the 8 known to be living, the average lapse of time since the diagnosis was established is five and a third months.

The effectiveness of irradiation as a palliative measure in selected cases is difficult to express in figures, and can be shown best by the following two cases.

*Presented at the annual meeting of the Massachusetts Medical Society on May 27, 1942.

†From the Department of Radiology, Massachusetts General Hospital.
‡Radiologist, Massachusetts General Hospital.

CASE 1. A 63-year-old man was admitted to the hospital on July 24, 1941, with a story of having been ill for 9 months. The illness had started with "pneumonia." The patient had lost 50 pounds in weight, and had a productive cough, which was severe, particularly at night. He complained of pain in the right shoulder, and difficulty in breathing when lying down.

Examination on admission showed cyanosis, without evidence of dilatation of the superficial veins; the breath sounds were slightly diminished over the entire chest, and the whispered voice was not transmitted. Dullness to percussion and tactile fremitus were absent. X-ray examination showed a lobulated mass in the region of the right hilum, with diminished aeration throughout the entire right lung field. These findings were considered to be consistent with primary bronchogenic carcinoma. The x-ray diagnosis was confirmed by bronchoscopy, and a biopsy taken at this examination showed oat-cell carcinoma.

X-ray therapy was advised, and the first treatment was given on August 5, 3 days after a definite diagnosis had been established. The treatment was given through two portals, one front and one back, centered over the mass; supervoltage x-rays were used. The patient received a total of 3000 r to the anterior and 2900 r to the posterior right chest. Treatments were given through a 12-by-12 cm. field in daily doses of 300 r. During the treatment, the patient developed a spiking temperature, which did not return to normal until 5 days after treatment was completed. In September, he received an additional 1500 r to each area. From that time on, improvement was continuous, and a second bronchoscopy with biopsy, done on December 12, 4 months after the treatment was begun, failed to show any evidence of disease. At the time of his last visit, April 22, 1942, the patient had no complaints, had gained considerable weight and was doing some work.

Comment. This patient had a very malignant, rapidly growing, radiosensitive tumor. He appeared for examination rather late in the course of the disease, but the diagnosis was made within 10 days, treatment was given promptly, and the immediate results were excellent.

CASE 2. A 64-year-old man was admitted to the hospital on June 10, 1941, complaining of cough and generalized weakness of 5 months' duration. The cough was productive of small amounts of blood-streaked sputum. The patient had a feeling of pressure in the left chest, some dyspnea and an intermittent wheeze, and had lost weight.

On examination, the chest appeared emphysematous, the trachea and heart being displaced to the left; the breath sounds were harsh on the left, but there were no rales or areas of dullness. X-ray examination showed collapse of the left upper lobe, with a marked shift of the trachea and mediastinum to the left. The cause of the obstruction was not clear. On June 16, bronchoscopic examination revealed a tumor at the orifice of the left-upper-lobe bronchus. The biopsy diagnosis was epidermoid carcinoma, Grade III.

Because of the patient's age and generally poor condition, surgery was not advised. He was not started on x-ray treatment until August 22, over a month after the diagnosis was made. The reason for the delay is not clear from the record. The treatment was given through two 10-by-10 cm. fields, one anterior and one posterior over the tumor. The daily dose was 300 r, and the total dose to each field 3000 r; supervoltage x-rays were used. Following the treatment, there was disappearance of symp-

toms, and an x-ray examination on December 3 showed re-expansion of the collapsed lobe and no visible tumor. A second bronchoscopic examination on December 5 showed no visible tumor; a biopsy was negative.

When last seen, on April 8, 1942, the patient was symptom free and looked well. X-ray examination, however, showed a small, rounded mass in the left 2nd interspace which may have been a recurrence.

Comment. This patient's life was made more comfortable and probably has been considerably prolonged by the treatment. Possibly, a better result could have been obtained if the delay between diagnosis and treatment had been avoided.

In both cases there is fairly definite evidence that it is possible to destroy the primary tumor with the treatment used.

DISCUSSION

Since the roentgenologic examination plays such a major part in the early diagnosis of cancer of the bronchus, I have attempted to group the cases according to their anatomic and histologic diagnosis in the hope that a better understanding of the basic pathological picture would improve the interpretation of the roentgenologic findings. Figure 1 is a schematic representation of the pathologic findings as demonstrated on the films. It is obvious that the roentgenologic appearance depends on the following factors: the location of the tumor, the type of tumor, the stage of the disease and the complications present.

The tumor may develop in one of the larger bronchi or in any of their more distal bifurcations, and its location determines whether it is seen as a central or peripheral shadow. It may grow outward into the lung substance, forming a more or less rounded, dense mass, with displacement of the adjoining bronchi away from the mass, or it may extend into the bronchial lumen, causing partial or complete obstruction of the bronchus. The latter type of tumor is more difficult to demonstrate roentgenologically, but it can often be seen as a mass within the bronchial lumen on films taken with the Bucky-Potter diaphragm, with the planograph, or after the injection of lipiodol.

More frequently, the presence of a tumor is suspected from the obstruction that it causes. The roentgenologic sign of bronchial obstruction varies with the degree of obstruction. When obstruction is partial, air enters the affected lung area with each inspiration, but its exit is prevented by the decrease in the bronchial lumen during expiration, and the area beyond the bronchial plug appears on the screen or film as a localized area of emphysema. If the obstruction is in a major bronchus, a shift of the heart and mediastinum away from the affected bronchus

occurs during expiration. This sign of bronchial obstruction is best demonstrated on films taken at the end of the expiratory phase, and may be

A persistent, low grade pneumonitis may develop, appearing on the film as an area of homogeneous density corresponding in size and

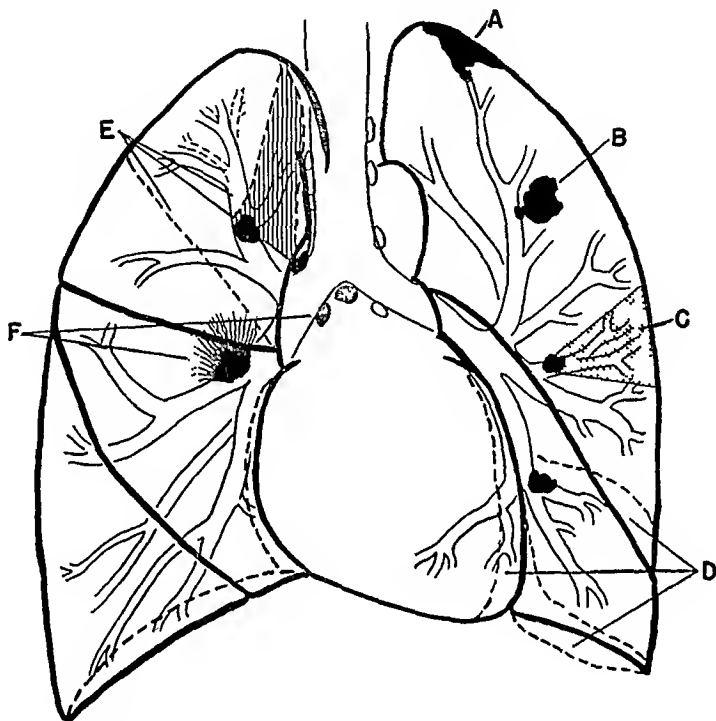


FIGURE 1

A—Early apical tumor arising in a terminal bronchus often called Pancoast tumor early symptoms—pain in the shoulder and sometimes Horner syndrome diagnosis made by aspiration biopsy B—Extraluminal bronchial tumor symptoms and physical signs absent, diagnosis made by surgical exploration C—Intraluminal bronchial tumor causing obstruction and obstruction pneumonia symptoms—cough and sometimes bloody sputum diagnosis made by bronchoscopy D—Intraluminal tumor causing partial obstruction, ball valve type with localized emphysema symptoms—same as in C diagnosis made by bronchoscopy E—Intraluminal tumor causing complete obstruction with collapse of the right upper lobe symptoms—cough, blood spitting and sometimes dyspnea diagnosis made by bronchoscopy F—Rapidly growing tumor with extension to regional nodes with or without signs of bronchial obstruction symptoms—same as in E diagnosis made by bronchoscopy

entirely missed when the examination is confined to films taken at full inspiration. As the lesion increases in size, and obstruction of the bronchus becomes more complete, one of the three following changes may take place in the area of lung supplied by the plugged bronchus

shape to the portion of the lung supplied by the involved bronchus

The part of the lung beyond the plug may become water logged (the so called 'drowned lung'), with subsequent infection, necrosis and abscess formation. In such cases, the shadow

seen on the film may have a somewhat mottled appearance, and cavities containing fluid levels may be demonstrated.

There may be a more or less complete col-

like or triangular areas of increased density replacing a lobe or a portion of a lobe. The lung adjoining the diseased area is unusually bright, owing to compensatory emphysema. The

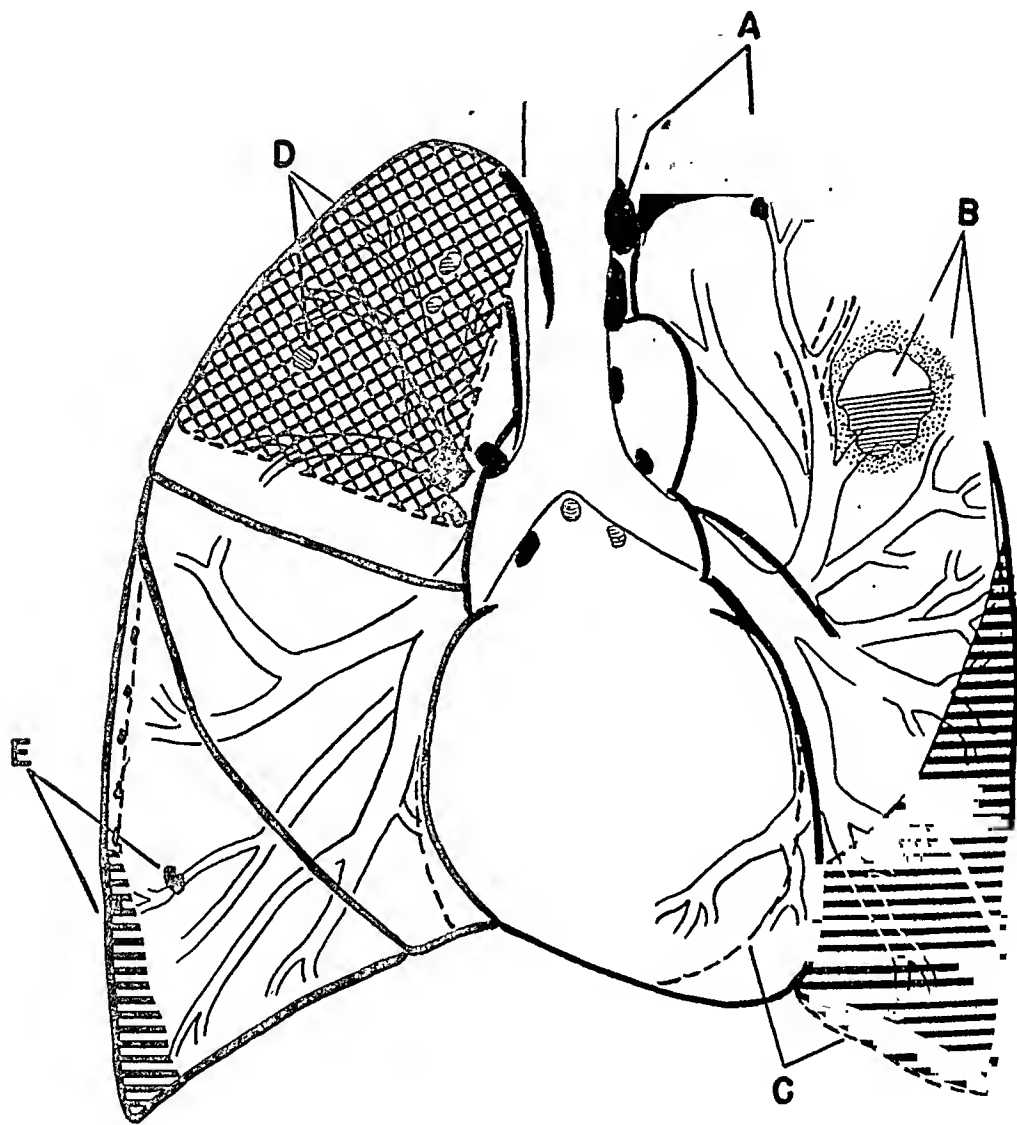


FIGURE 2.

A—Advanced apical tumor with extension to pleura and regional nodes; symptoms—cough, pain in shoulder, radiating down arm, and, usually, Horner syndrome; sometimes, signs of phrenic-nerve paralysis. B and C—Large extraluminal tumor with necrotic center, involvement of the pleura, fluid in the pleural space and foul and often bloody sputum; pieces of tumor may be coughed up; may be mistaken for lung abscess. D—Intraluminal tumor with complete block and drowned or necrotic lung, which may contain small cavities; sputum may be foul; fever and other signs of infection present. E—Small peripheral tumor with direct extension to the pleura; pleuritic pain and small amount of fluid in the pleural space; diagnosis made by thoracoscopy.

lapse of the lung distal to the plug. The roentgenologic appearance varies according to the size of the area involved, the completeness of the collapse and the length of time it is present. These collapsed areas are usually seen best in the lateral view of the chest, when they appear as band-

interlobar septums, when visible, are displaced toward the collapsed area. When an entire lobe is involved and the process is not of too long standing, there is a shift of the heart and mediastinum toward the affected side during inspiration.

Removal of the plug may result in a return of the lung to its normal appearance. It should not be forgotten that the commonest cause of bronchial obstruction is not carcinoma, or that a benign adenoma may be confused with a malignant tumor.

The histologic characteristics of the tumor play a part in determining the roentgenologic appearance, but a less significant one than the location of the tumor. The oat-cell and undifferentiated carcinomas rarely if ever produce rounded, sharply defined masses outside the bronchial lumen, although they not infrequently involve the lung, being seen as poorly defined, irregular shadows extending outward from the affected bronchus.

When the disease is far advanced, after it has extended beyond the regional lymph nodes, or when there is widespread infection with fluid in the pleural space, the picture is dominated by these secondary manifestations, and roentgenologic examination may be of little value in determining the underlying cause. At this point, reliance should be placed on other methods of diagnosis.

A knowledge of the usual distribution of the metastases in carcinoma of the bronchus is of considerable advantage in the interpretation of the roentgenologic findings and of the clinical symptoms. Enlargement of the peribronchial and peritracheal lymph nodes occurs relatively early, and should always be looked for. This enlargement is of diagnostic value and has a direct bearing on the question of operability. Extension to the pleural surfaces seems to occur more frequently.

If the tumor arises in a minor bronchus, it is situated near one of the interlobar veins. With massive involvement of the lymph nodes, the phrenic nerve may be involved, and roentgenologic examination will show elevation of the diaphragm on the affected side. When the pleura is involved, there is usually evidence of fluid in the pleural space, and nodules on the pleural surface can sometimes be demonstrated after artificial pneumothorax. Clinically, these patients complain of pleural pain, and if the process is at the apex they may have a Horner syndrome. Metastasis to bone is not uncommon, but the roentgenologic appearance does not differ materially from that seen in other metastatic bone tumors. Metastasis to the brain, liver, adrenal glands or mesenteric lymph nodes occurs very often, and may give rather characteristic symptoms, although the masses are not usually demonstrated on the film. When the disease is complicated by an extensive infectious process, the roentgenologic appearance is that of infection, and the underlying tumor may

be overlooked. The differentiation of these tumors from other obstructing lesions of the bronchi, from pulmonary metastasis of tumors arising in other parts of the body and from benign tumors of the bronchi is largely dependent on the clinical history and the bronchoscopic examination. The worth of roentgenologic examination is in the demonstration of a lesion consistent with carcinoma of the bronchus to the end that other more complicated diagnostic methods may be undertaken.

Before these patients are subjected to irradiation, the diagnosis should be definitely established, preferably by biopsy. Benign tumors should be ruled out, since the surgical results in this group are excellent and only harm can result from irradiation. No case in which there is a reasonable chance of complete surgical removal should receive roentgenologic treatment, and cases in which extensive metastases have already occurred, or in which massive infection is present, are probably better treated by other means.

The cases in which benefit from irradiation may be expected are those with oat-cell or undifferentiated carcinoma without definite evidence of metastasis beyond the regional lymph nodes. This is a rather large group.

The evidence of benefit from irradiation in these cases is not conclusive, but it is an advantage in the treatment of these tumors.

In my presentation, I have seemed to place emphasis on the use of the roentgen ray in the diagnosis and treatment of bronchogenic carcinoma, it is not because I do not appreciate that medicine and surgery play the major part in the problem, but because the roentgen ray is the part in which I am most interested and because it has received less attention. The medical and surgical aspects have been covered thoroughly by other physicians at the Massachusetts General Hospital, and I am very much indebted to them for permission to use their material.

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THE PLACE OF GASTRODUODENOSTOMY IN THE SURGERY OF DUODENAL ULCER*

HOWARD M. CLUTE, M.D.,† AND JOHN S. SPRAGUE, M.D.‡

BOSTON

FOR some years, the consensus has been that simple duodenal ulcer is primarily a medical problem, and it is well known that 80 to 90 per cent of duodenal ulcers can be satisfactorily managed by medical treatment. When complications occur in the course of a duodenal ulcer, however, surgery is necessary. The chief complications of duodenal ulcer that may require surgery are acute perforation, hemorrhage, pyloric obstruction and a failure of medical measures to give satisfactory relief of symptoms.

In past years, the majority of surgeons employed a short-circuiting operation for duodenal ulcers that had developed any of the above complications. In many cases, lasting relief was obtained by this procedure. As time went on, however, it became increasingly evident that the frequency of gastrojejunal ulceration after posterior gastroenterostomy was great and that this lesion was more trying than the original ulcer. Surgical opinion turned more and more to subtotal gastrectomy as the procedure of choice in complicated ulcers. It is now generally believed that, when possible, a resection of two-thirds or more of the stomach, which must include the pylorus, is best in the treatment of duodenal ulcers with hemorrhage or intractable to medical treatment. We are in complete accord with this opinion. In our clinic, patients with duodenal ulcers who have failed to gain relief from careful medical treatment are subjected to radical subtotal gastrectomy; patients who have had repeated hemorrhages from the

duodenal ulcer are likewise subjected to gastric resection when operative interference is deemed necessary.

In 1938, we§ described the technic and reported the results in a small group of cases of duodenal ulcer in which a gastroduodenostomy, instead of a posterior gastroenterostomy, had been performed. The results were uniformly good, but we realized that sufficient time had not elapsed after the operation to make the report especially significant.

The 15 cases reported in 1938 and 11 more cases since then have been followed to date. It is our opinion that we are beginning to have some definite information regarding the dangers and complications that may follow gastroduodenostomy and the benefits that one may anticipate from this procedure. From these facts, the indications for gastroduodenostomy in certain duodenal ulcers may be decided.

In our experience, pyloric stenosis following a long-standing duodenal ulcer is completely and permanently relieved by gastroduodenostomy. For many years, it has been known that the best results of posterior gastroenterostomy have followed its use as a short-circuiting procedure in duodenal ulcers that had produced a fibrous stenosis of the pylorus. The question arises, Why should one use gastroduodenostomy in these cases instead of the time-tried posterior gastroenterostomy? We prefer gastroduodenostomy because it is more easily and simply performed and has less immediate postoperative complications. Furthermore, in our cases, there has not been, as yet, even a suggestion of later jejunal ulceration. Finally, it

*From the Surgical Service, Massachusetts Memorial Hospitals.

†Professor of surgery, Boston University School of Medicine; surgeon-in-chief, Massachusetts Memorial Hospitals.

‡Assistant in surgery, Boston University School of Medicine; assistant surgeon, Massachusetts Memorial Hospitals.

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has long seemed to us that normal physiology was more closely approximated when the acid gastric contents were emptied into the second part of the duodenum than when they were poured into the jejunum

In the previous paper, we reported 7 patients with pyloric stenosis treated by gastroduodenostomy. We have recently reexamined all these patients. They are without exception perfectly well, so far as their digestive apparatus is concerned. They eat as they wish, and have no indigestion or distress. Since our last report, we have done eleven more gastroduodenostomies for pyloric stenosis, all these patients are well, with no digestive troubles. Thus, 16 patients with obstructing duodenal ulcers have been treated with gastroduodenostomies and followed from a few months to seven years with such satisfactory results that we are deeply impressed. We realize that this is a small group of patients and that half of them have been followed less than five years. However, this carefully followed group does give a definite suggestion that gastroduodenostomy may be preferable to other short circuiting operations in obstructing duodenal ulcers. We are completely satisfied that the procedure is preferable to subtotal gastric resection for these patients, who are usually old and whose body chemistry is seriously altered by their pyloric stenosis.

We have used gastroduodenostomy in the surgical management of two gastrojejunal ulcers that followed posterior gastroenterostomy. One of these patients was fifty five and the other fifty nine years of age. Both entered the hospital with active serious hemorrhage from the gastrojejunal ulceration and presented a very serious surgical problem. We agree that the ideal procedure in the management of gastrojejunal ulcer is removal of the loop of jejunum and its stoma from the stomach, closure of the jejunum by suture of the orifice or end to end anastomosis, resection of the stomach and performance of an anterior or posterior Polya type of anastomosis.

The third part of the procedure, in our experience, may be more than the patient can safely bear, since this resection must follow the removal of the jejunum from the stomach and its suture. We know that it is dangerous to remove the jejunum, close it and close the gastric defect, and do nothing to the duodenum, even though the duodenal ulcer seems to be quiescent. Reactivation of the duodenal ulcer, with hemorrhage, perforation or obstruction, occurs too frequently under these conditions. In these 2 patients, treated seven and six years ago, a gastroduodenostomy was quickly and readily done after the bleeding gastrojejunal ulcer was excised and the stomach and jejunum closed. Both patients

have been followed to date and are quite free from digestive troubles. We believe that, under circumstances such as these, gastroduodenostomy rather than partial gastrectomy may be a lifesaving procedure. We shall have no hesitation in carrying out this operation in future patients with gastrojejunal ulcers who are poor risks.

We do not consider gastroduodenostomy the method of choice for the surgical management of a bleeding duodenal ulcer, in which resection of the ulcer and a radical resection of the stomach should be done, if any surgery is undertaken. We did a gastroduodenostomy for a bleeding duodenal ulcer in 1935. The patient died a few hours after operation. This is the only death we have ever had following gastroduodenostomy. In 1936, we did a second gastroduodenostomy for a duodenal ulcer with repeated hemorrhages. This patient is well, six years later, and has no digestive trouble.

We do not believe that gastroduodenostomy is a procedure of choice in the surgery of gastric ulcer, although we have twice used it in conjunction with local excision of the lesion. Both patients are now well, one seven years and the other four years after operation. In each of these cases, the ulcer was very high on the lesser curvature of the stomach, and its removal would have necessitated almost a total gastric resection. One of the patients has had several trying bouts with recurrent gastric ulcer since operation, but since he is now well he will not consider reoperation. The other patient has remained well. It is perhaps true that in certain very high gastric ulcers, local excision of the ulcer and gastroduodenostomy will prove satisfactory, but, in general, a radical subtotal gastrectomy is preferred in these cases.

Certain duodenal ulcers cause distress and disability in spite of long-continued and careful medical treatment. These patients, in our opinion, should have radical subtotal gastric resections and neither posterior gastroenterostomy nor gastroduodenostomy. In such patients, high gastric acidity is common preoperatively and gastrojejunal ulceration postoperatively, unless the gastric antrum and most of the acid secreting gastric glands are removed surgically.

We have done gastroduodenostomies in 4 patients because of the failure of medical treatment. One of these patients—and the only case in our series—cannot be traced. Two have remained well and have no digestive troubles four and five years, respectively, after operation. The fourth patient has about as much indigestion now as she did before operation, and she represents the only known failure in the series. Since operation, she has gone through a divorce and has also lost her mother. Her diet is entirely unsatisfactory. We are

at present following her in the Gastro-Intestinal Out Patient Department with the hope that a proper diet will give relief. There is no evidence of a stomial ulcer in this case. We have every reason to believe that our own judgment was at fault in selecting the surgical procedure.

SUMMARY

Twenty-six gastroduodenostomies have been performed for the complications of duodenal ulcer, with one death. One case has been lost, but the remaining 24 have been followed to date.

In 16 cases of organic pyloric stenosis, the results have been so entirely satisfactory that we have been greatly impressed with the value of the operation in this condition.

Two patients with bleeding gastrojejunal ulcers were treated by resection of the jejunal ulcer and closure of the jejunum and stomach; a gastroduodenostomy instead of a gastric resection was done because of their condition. Both patients have remained well for many years. Under these

circumstances, we believe gastroduodenostomy may frequently be a lifesaving procedure.

We do not recommend gastroduodenostomy for the treatment of serious hemorrhage from duodenal ulcer or when medical treatment has failed; subtotal gastric resection is the operation of choice for these conditions.

Only rarely is gastroduodenostomy, in combination with local excision of an ulcer high on the lesser curvature of the stomach, employed. In some cases, however, this conservative procedure may well be preferable to a total or nearly total gastrectomy for these lesions.

In our experience, gastroduodenostomy is even more easily done than posterior gastroenterostomy, and certainly the patients have a smoother post-operative course. No gastrojejunal ulceration has followed gastroduodenostomy in our experience. This seems logical, since in gastroduodenostomy the acid gastric secretion empties into the duodenum, which is prepared for it, rather than into the jejunum, which is not.

CLINICAL NOTE

A DEVICE FOR THE INTERNAL FIXATION OF BONE

LYMAN SMITH, M.D.*

BARRINGTON, ILLINOIS

INTERNAL fixation of bone is rapidly coming into more general use in the treatment of fractures. The surgical and physiologic problems have been fairly well solved. The mechanical aspects of this engineering problem, however, are of equal importance and have recently been receiving an increasing measure of attention. In 1938, Hawley and Padula¹ introduced an angle plate that does not bend; Murray² advocated the use of a transfixion screw crossing the fracture site in conjunction with the usual plate. Lyon, Cochran and Smith³ tested the holding power of various types of screws used in bone and determined the correct size of drill for each. All this work was directed toward increasing, as much as possible, the efficiency of the internal immobilization. It is the purpose of this paper to present a device that is mechanically more efficient than the screws in present-day use.

The device, illustrated in Figure 1, is a screw-type expansion sleeve.[†] It consists of two parts:

*Formerly, resident, Bone and Joint Service, Boston City Hospital.

[†]The development of this device is due, in large part, to the generous co-operation of the Illinois Tool Company, Chicago.

a small screw threaded about half its length, and a sleeve member into which the screw is seated. The sleeve is slit into four sections, which are so tapered that, when the leading point of the screw engages them, they are forced open and thus form a wedge.

Up to the present time, this device has been used only in cancellous bone, to which it is applied in the following manner: a 6/32-inch hole is drilled to the desired depth, and an expansion sleeve of the proper length is then selected and inserted into the drill hole; the head of the sleeve is grasped with a forceps to prevent rotation, and the screw member is then seated with a small screw driver.

Delay in obtaining machine tools has prevented its use in cortical bone. Obviously, the sleeve sections of the device cannot expand against such hard material as cortical bone; instead, therefore, one must use a tool that will enter a drill hole on the exposed surface of a bone and ream out a wider bore below the surface, equaling the diameter of the expansion sleeve. One such instrument has been designed and used experimentally, but is not yet perfected.

The mechanical principle underlying the expansion sleeve is not new, since similar fasteners are used in cement and brickwork.

The holding power of a nail or screw in soft cancellous bone is not great. In experimental animals, however, these sleeves averaged 40 per cent more holding power in cancellous bone than

coarse deep threaded screw. This added fixation is of advantage in allowing early motion after

the screw, whereas the opposite is true of the expansion sleeve. For this reason, absorption of

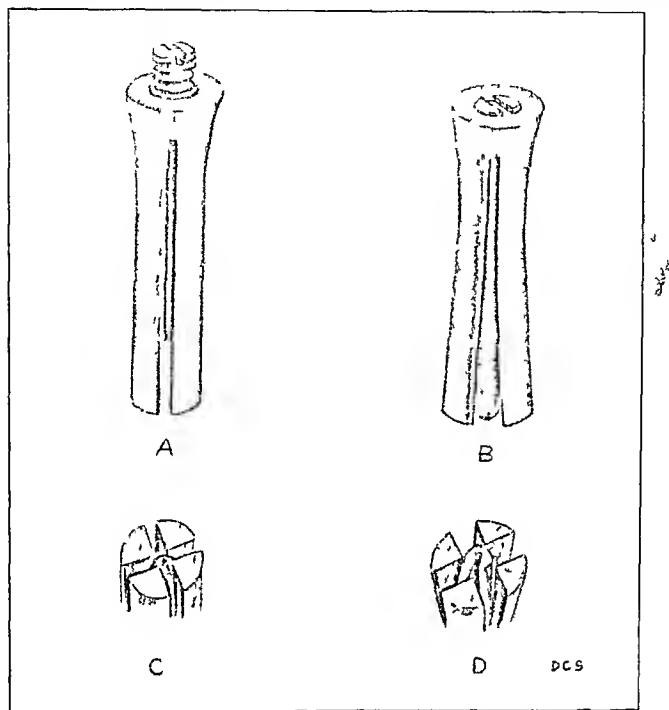


FIGURE 1 *Screw Type Expansion Sleeve*

A—Expansion sleeve closed, screw not seated B—Expansion sleeve opened, screw seated, forcing sleeve sections open C—Distal end closed D—Distal end opened

reduction, which is desirable in fractures around joints.

Venable, Stuck and Beach⁴ have proved that resorption of bone around screws made of alloys, other than vitallium, is caused by electrolytic irritation. The stresses produced about a screw, however, also result in absorption of bone and subsequent loosening. Figure 2 illustrates the stresses around a screw and around an expansion sleeve, both used to fasten together two pieces of Marblette, a phenol resin plastic that has a high photoelastic property to show strain effects produced by concentration of pressure. The magnitude of these stresses is dependent on the number of dark and light lines concentrated at any one point or area. The photograph shows that the stresses are very prominent and concentrated about

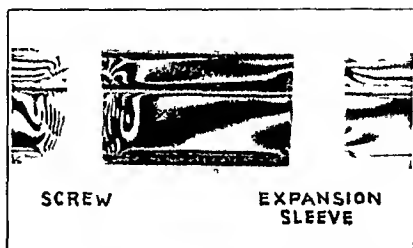


FIGURE 2 *Lines of Stress about a Screw and an Expansion Sleeve*

bone about the expansion sleeve is slower and less marked than that about a screw.

Removal of an expansion sleeve weeks after insertion, when it had served its purpose, might be thought difficult because of the formation of

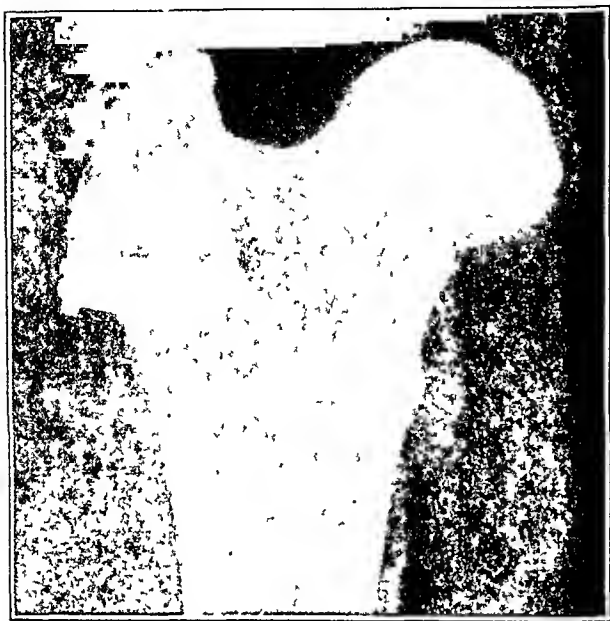


FIGURE 3. *Expansion Sleeve Six Weeks after Insertion in a Dog's Femur.*

callus between the screw member and the expanded sleeve sections. This has not proved to be so. Figure 3 shows an expansion sleeve

buried for six weeks in the greater trochanter of a dog's femur. There was no absorption of bone about the sleeve, which, on examination, was found to be seated firmly. After the screw member had been turned out, the sleeve was easily extracted. Expansion sleeves in place as long as ten weeks have likewise been easily removed.

Since accurate machining of this device is necessary, it cannot be made from such a hard alloy as vitallium, which must be cast. However, the new S-Mo (Enduro) stainless steel has been found to be practically as inert in the tissues as vitallium. If the expansion sleeve were manufactured from stainless steel in large numbers, its cost would probably not exceed that of a vitallium screw.

SUMMARY

A new device for the internal fixation of bone is presented. It is simple to apply, exhibits greater holding power than a screw and creates fewer lines of stress in the bone about it. It has no apparent disadvantages.

Brinker Road

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MEDICAL PROGRESS

CARCINOMA OF THE PROSTATE

WILLIAM C. QUINBY, M.D.*

BOSTON

ANY consideration of the subject of carcinoma of the prostate must emphasize once again the frequency of its occurrence in all men past the age of fifty years. From the clinical viewpoint, it has long been recognized that in about 20 per cent. of all male patients of this age who have symptoms of prostatism, these symptoms are found to be due to a prostatic carcinoma. More recent inquiry into the incidence of prostatic carcinoma comes from routine post-mortem examination by the pathologist, by which additional cases of cancer are demonstrated in many patients dying from various other conditions who showed no evidence of prostatic carcinoma during life. Thus, Moore¹

finds carcinoma of the prostate in 17 per cent of all men over fifty years, and this incidence increases steadily with age, until it reaches 29 per cent in patients who are in the ninth decade. The disease probably originates in cells that have previously undergone atrophy of a senile type. A more recent study of this subject by Kahler² at the Mayo Clinic has given similar figures. His observations were derived from 195 cases. In 72, the diagnosis was made ante mortem; in 69, the carcinoma was discovered only at autopsy; and in 54, it was found only by a more detailed study of sections in cases that had previously been considered benign both clinically and pathologically. The clinical diagnosis was made by palpation in 23 cases, by palpation and biopsy in 30 cases, and by the presence of characteristic distant metastases in 19 cases. The average age of these patients

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress Annual*, Vol. III, 1942 (Springfield, Illinois: Charles C. Thomas Company, 1942 \$5.00).

*Clinical professor of genitourinary surgery, emeritus; urological consultant, Peter Bent Brigham Hospital

was sixty-five years, and the total incidence of carcinoma 17.3 per cent. Of tumors recognized either clinically or grossly at necropsy, 54 per cent had produced metastases. So far as the point of origin of the neoplasm in the prostate is concerned the lateral and posterior lobes were most frequently involved. The growth never arose in the median lobe. In several cases, its origin appeared to be "multicentric." The type of tumor was squamous cell in 3 per cent of the cases and adenocarcinoma in the others, whose malignancy was classified as Grades I and II in 69 per cent. This, of course, reflects the clinical experience that prostatic cancer is a slowly growing type of tumor on the whole, spreading most frequently by metastases, rather than by invasion of contiguous structures.

Regarding the manner of extension of the original growth, the perineural lymphatics were found to contain cells in all cases in which the tumor was of the more malignant types—Grades III and IV—and in 91 per cent of all tumors investigated, regardless of type. Therefore, if one considers this evidence conclusive, one must agree with Kahler that "it makes very questionable the possibility of operative cure." Moore¹ also called attention to this frequent invasion of the perineural lymphatics, even in early stages of the disease. Further investigation into the mode of spread of carcinoma of the prostate has been carried out by Warren and his co-workers.³ Although transport by means of the blood stream is undoubted, they believe that the perineural lymphatics offer the tumor an additional way of access to bone and that this fact accounts for the marked frequency with which the bony pelvis and lower vertebrae become involved, as compared with regions more distant from the tumor.

Such observations as these, combined with the insidious progress of the growth that makes early clinical recognition of its presence infrequent, have led to a rather widespread attitude of defeatism concerning the operative treatment of prostatic carcinoma, which is often unjustified. It is to be remembered always that the pathologist can describe with accuracy only what he sees in the individual microscopic slide. Beyond this, conclusions regarding cause and effect may easily be fallacious. It is wrong, for example, to assume that a tumor cell lying apparently free in a tissue space surrounding a nerve is undergoing transport in a direction away from its point of origin. Furthermore, the term "perineural lymphatic" is not at all accurate, for the accepted connotation of "lymphatic" is that of a tubular structure walled by endothelial cells, a part of the general lymphatic apparatus of the body. The implication is that there is a progression of the fluid or lymph con-

tained in such a lymphatic in the direction of the more central areas of the body, the current being similar to, although slower than, that in the capillaries leading to veins. The areas about the very numerous sympathetic nerve fibrils with which the prostate is supplied are really only tissue spaces—lymph spaces, possibly, but certainly not true lymphatics. That a cancer cell lying in such a space about a nerve fibril will be viable on transportation to some distant point of the body, or is even being so transported, is not proved by any evidence at hand. Metastasis by way of the blood stream, especially by the veins, is of course acknowledged, but that these cells in proximity to nerve fibrils play a significant part in the spread of the neoplasm is yet to be demonstrated. Certainly, the clinical evidence afforded by the recorded cures after total prostatectomy, together with the well-known slow progress of prostatic carcinoma in general, suggests strongly that this perineural invasion is of little prognostic significance. The observations of Warren and his associates were derived from autopsy and thus represent only the terminal picture of the malignant process.

A valuable aid in the study of prostatic carcinoma has been the result of examination into its relation to the enzyme phosphatase present in tissues and appearing also in the serum of the blood. This enzyme, acting as a catalyst, has the power of liberating phosphate ions from phosphoric acid esters. The amount so liberated depends on the reaction of the solution in which it takes place. Thus, the optimum pH for the alkaline phosphatase is 8.6, whereas that for the acid phosphatase is 4.8 to 5.0. The reaction is expressed in units per 100 cc. of blood serum.

Following the demonstration on phosphatase by Bodansky⁴ and that by Kutscher and Wolbergs,⁵ which showed that prostatic tissue contains a large amount of acid phosphatase and but little alkaline phosphatase, the Gutmans⁶ have studied this subject extensively. They found that the prostate in the newborn contained 4.5 units per gram of tissue; that of a boy of four years, 1.5 units; and that of a boy of thirteen years, 73 units; whereas the prostate of the adult man showed much greater phosphate activity, varying from 522 to 2284 units. Evidently, therefore, the content of the prostate in phosphatase bears a definite relation to its maturity, increasing markedly after puberty and represents a secondary sex characteristic of a chemical nature. In the blood serum of normal persons, the amount of acid phosphatase activity was found to be from 0.5 to 2.5 units per 100 cc. In patients with bone metastases from prostatic carcinoma,

however, a very marked increase in the amount of acid phosphatase in the blood serum takes place, whereas in the serum of patients with prostatic carcinoma but no metastases, the phosphatase readings are normal.

Gomori⁷ has devised special staining methods by which it is possible to demonstrate phosphatase in tissues. Prostates containing carcinoma when so stained show an abundant black deposit, owing to the large amount of phosphatase present.

The important studies on the relation of the prostate to the various endocrines, and especially to the sex hormones, undertaken by Huggins and his collaborators⁸⁻¹³ at the University of Chicago have had an especially significant result in the field of therapy of carcinoma of this gland. An operation was devised by which the prostate of dogs was separated from the urinary tract so that prostatic activity could be studied over long periods in response to various conditions or injections. Determination of prostatic activity was made after the collection for one hour of the secretion caused by an injection of 6 mg. of pilocarpine. Castration of such dogs was followed by marked and increasing reduction and eventual cessation of the prostatic secretion in from seven to twenty-three days. After this, the secretion could be re-established by the injection of testosterone. This depression of prostatic secretion after removal of the testes, well recognized for years in both man and animals, therefore depends on the reduction of the male sex hormones, the androgens, of whose greatest amount the testis is the origin. The concept then followed that prostatic carcinoma, being composed of epithelial cells of a mature type, might be responsive to a depression of the androgenic hormones in the organism, in common with all other types of adult prostatic epithelium. Using the phosphatase estimation as a method of objective proof of the concept, these workers found that androgen injection caused a marked rise of acid phosphatase in patients with prostatic carcinoma and that castration or estrogen (female sex hormone) injection produced a sharp decrease in the activity of the phosphatase.

Twenty-one patients with advanced prostatic cancer were castrated, and the clinical effects observed during twenty months. Four of the men died, and in 2 the clinical results were reported as unsatisfactory. The authors further state:

In those patients who were improved the more objective clinical evidence of tumor regression consisted of increased appetite and a progressive gain in weight; improvement in red cell and hemoglobin values; decrease in pain and objective neurological symptoms (2 patients who had compression of the cauda equina with a complete block of the subarachnoid space had a restoration of the circulation of cerebrospinal fluid and resolution of the paralytic and anesthetic changes

following castration); decrease in the size of the primary tumor on rectal palpation and at cystoscopic examination; stabilization or regression of bony metastases in roentgenograms; and a decrease in the size of palpable lymph nodes which were the site of metastatic cancer. It was our opinion that complete regression of the tumor had not taken place, although the depression of the tumor activity with resulting improvement of the patient in some cases was considerable. In about 20 per cent of the cases the results were unsatisfactory. Further observations found that the administration of stilbestrol reduced still further the level of the acid phosphatase below that reached after castration. Estrogen is therefore found to supplement the action of lowering the androgens of the body brought about by castration.

Following this very important report made at the meeting of the American Urological Association in May, 1941, many patients with prostatic carcinoma have been subjected to orchidectomy, with results that in some cases have been quite phenomenal. The most striking benefit was usually the relief of conditions caused by the metastases: in several well-authenticated cases, the patient, partially paralyzed by pressure on the spinal cord and nerve roots, was freed from pain and again able to walk. That orchidectomy does not result in a total resolution of the cancer in the prostate itself seems to be generally acknowledged. Nevertheless, there is no doubt that this procedure relieves many of the most prostrating symptoms of the sufferers.

Other methods of reducing the androgens in the body are exposure of the testes to the destructive action of the x-ray and the use of an estrogen, such as diethylstilbestrol. Munger¹⁴ reports a series of cases of prostatic carcinoma treated by resection followed by irradiation of the testes. He believes that such x-ray treatment has given some added benefit, but his results do not seem very convincing. Herrold¹⁵ reports 12 patients with cancer of the prostate to whom diethylstilbestrol was given. A consistent result was seen in the relief of pain. Also, the patients showed an improvement in general condition and, in some cases, a gain in weight. Rectal palpation in one patient who had taken the drug to the amount of 350 mg. during a period of five and a half months showed a diminution in the size of the growth of about 50 per cent and a diminution in its hardness. Pain in the breasts, with some increase in size (gynecomastia), was the only untoward result of the administration of the drug in daily doses of 3 mg. The effects following testicular irradiation or diethylstilbestrol, however, in no case are reported to be so outstanding as those seen after orchidectomy.

It is of interest, in view of the newer knowledge of the sex hormones and their effect on castration, to consult the early opinions concerning this procedure as a method of treating the enlarged and

obstructing prostate. Before the American Surgical Society, in 1893, White¹⁶ read a paper advocating orchidectomy for the hypertrophied prostate after having demonstrated that this operation causes atrophy of the prostate in dogs. Three years later, Cabot¹⁷ presented to the same society an analysis of the clinical results of this operation in man. No distinction was made between a benign and a malignant hyperplasia of the prostate. The results on the whole were poor, although an occasional case was found in which the improvement in the patient's condition and ability to empty the bladder was marked. It was probably the malignant prostate in which a favorable reaction to operation was obtained.

Those who advocate total removal of the gland whenever possible are increasing steadily. There is no longer any doubt of the excellent results of such removal in cases in which the diagnosis has been made sufficiently early. The recent papers of Colston¹⁸ and of Lowsley and Kilgore¹⁹ bear witness to this fact. For patients in whom the carcinomatous invasion is too extensive to permit a total prostatectomy, resection of the obstructing portions by way of the urethra is of inestimable value, as brought out in the paper of Wishard, Hamer and Mertz.²⁰ The use of radium either in the form of the salt or as emanations in "seeds," rather general a few years ago, today finds fewer advocates.

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Recent advances in the knowledge of the biologic characteristics of carcinoma of the prostate have already resulted in markedly increasing ability to relieve the symptoms of sufferers from this disease. A defeatist attitude today is entirely unjustified.

Continued emphasis must be placed on the early detection of the carcinomatous prostate by rectal examination of men fifty years of age and older as an important part of an annual physical examination. Because of the insidious progress of this disease, in no other way will the number of cases amenable to total removal of the gland be increased, and to date this is the only method of cure.

A more general use of the biopsy in every suspected case is strongly advised, even though at times this necessitates an exposure of the prostate through the perineum.

Patients with prostatic carcinoma should be studied at frequent intervals, both before and after operation, by estimation of the phosphatase activity of the blood serum and by x-ray study of the spine and pelvis as indices of their condition.

The growth of prostatic carcinoma is retarded by a reduction of the amount of androgenic sub-

stances present in the body. Such a reduction is brought about primarily by castration, and secondarily, and to a much less degree, by the administration of one of the estrogens, preferably diethylstilbestrol.

A suggested course of treatment of patients with prostatic carcinoma is as follows: for patients with few or no urinary symptoms but with an amount of carcinomatous invasion too extensive to permit total prostatectomy, castration, followed by diethylstilbestrol is advised; for those with obstructive symptoms and a degree of malignant invasion too extensive for total prostatectomy, transurethral resection, combined with castration, is preferred; in patients for whom total prostatectomy can be done but who already have metastases, prostatectomy, followed at least by stilbestrol, and possibly by castration if the acid phosphatase remains high, should be performed; patients amenable to radical excision of the gland should have operation, followed by careful observation of the phosphatase readings, castration being reserved until high values of this enzyme indicate its need.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28401

PRESENTATION OF CASE

First admission. A six-month-old male infant was admitted to the hospital because of cough, vomiting and a shrill cry.

Three weeks prior to entry, the child began to vomit his feedings immediately after ingestion. During this time, he developed a cough productive of small amounts of sputum. This did not occur in paroxysms and was not similar to the cough of whooping cough. However, vomiting often occurred after coughing. The physician did not find the temperature elevated, but the child seemed to perspire, particularly about the head. The symptoms were unaffected by variation in the feeding formula. During the three days before admission, the child vomited everything consumed, and the vomiting was termed "almost projectile." He became quite constipated and lost 2 pounds.

The family history was irrelevant. Two siblings, aged four and two years respectively, were well.

Born at term after a normal spontaneous delivery, the patient was declared "a small baby," but was vigorous and quite normal. The development was normal, and the diet adequate.

Physical examination revealed a pale, poorly nourished, slightly dehydrated, weak, flabby infant with a high-pitched, feeble cry. The throat was slightly congested and filled with mucus. The heart and lungs were normal. The abdomen was soft and scaphoid. The liver edge was felt 1 or 2 cm. below the costal margin. Neurologic examination was negative.

The temperature was 99.2°F., the pulse 150, and the respirations 30.

Examination of the blood revealed a red-cell count of 2,350,000 with a hemoglobin of 40 per cent, and a white-cell count of 7400 with 43 per cent polymorphonuclears and 57 per cent lymphocytes; the hematocrit was 23 per cent. The blood Hinton reaction was negative. Examination of the urine was negative. X-ray examination of the long bones, skull and chest was negative. The tuberculin test was negative.

The child was treated with physiologic saline infusions, blood transfusions and a gradually increased formula. The anemia cleared. The patient was discharged after seventeen days, apparently improved.

Second admission (eight days later). The mother stated that on the day of discharge from the hospital she noticed that the patient's fingers and toes were blue. On the second day after discharge, he began to vomit after feedings, although the hospital formula was followed. At times, a refeeding was not vomited, and water could be tolerated. The patient lost interest in his toys, lay quietly and fussed when picked up. A week later, he was found breathing with difficulty, and the fingers were blue. This became progressively worse, and a day later, he was readmitted to the hospital. He was said to have gained 12 ounces since discharge.

Physical examination revealed a pale, fretful, slightly dehydrated infant, who showed little interest in his surroundings and who cried when moved. The face and nail beds of the fingers and toes were blue. The fontanelles were soft and were not sunken. The throat was moderately congested and filled with mucus.

Examination of the heart revealed only a tic-tac rhythm. The lungs seemed clear anteriorly, but showers of fine rales were heard in both upper lobes posteriorly and the chest seemed dull to flat in these areas. The abdomen was somewhat protuberant and tympanitic, and the umbilicus protruded. The liver edge was felt 3 cm. below the costal margin. The spleen was not felt.

The temperature was 102°F., the pulse 160, and the respirations 60 to 80.

Examination of the blood revealed a red-cell count of 4,000,000 with a hemoglobin of 87 per cent, and a white-cell count of 51,000 with 55 per cent polymorphonuclears. The following day, the white-cell count was 18,400 with 79 per cent polymorphonuclears. There was a marked anisocytosis, and many normoblasts were present on the blood smears. There was no sickling of the red cells. In the fragility test, no hemolysis occurred at 0.50 per cent, and at 0.25 per cent there was complete hemolysis. The carbon dioxide combining power was 15.7 milliequiv. per liter, and the nonprotein nitrogen was 20 mg. per 100 cc. The throat and stool cultures were negative for pathogenic organisms.

X-ray films of the bones showed no evidence of disease. The chest was described as being unusually large. The diaphragm was low in position. The size and shape of the heart showed no variation from the normal. No unusual masses were seen. The trachea and main bronchi were

clearly visible and appeared normal. In the fluoroscopic examination, the mediastinum appeared shifted to the left, but there was no respiratory change. The pulmonary markings were increased on both sides.

An electrocardiogram on the second day after admission showed a sinoauricular tachycardia, with a rate of 150 per minute. The PR interval was 0.12 second. There was a moderate right-axis deviation. Electrocardiographic studies done three and twelve days later revealed no significant change.

The patient was maintained quite well in an oxygen tent but became quite cyanotic when removed. On the eighth day, the red-cell count was 5,100,000 with 100 per cent hemoglobin, and the white-cell count was 11,200. He continued to gain weight. A marked pitting edema was noted on the eleventh hospital day, and clubbing of the fingers seemed to have developed. The liver became enlarged until the edge was felt at the crest of the ilium. On the day of death, the patient was removed from the oxygen tent for a bath. He became quite cyanotic and remained so after being returned to the oxygen tent, contrary to what had previously occurred. He died forty-five minutes after being returned to the tent.

DIFFERENTIAL DIAGNOSIS

DR. CONGER WILLIAMS: In summary, this infant entered the hospital for the first time because of an acute episode characterized by vomiting, cough and severe anemia from which he apparently recovered in seventeen days. A second episode starting eight days after discharge and characterized by vomiting, dyspnea, cyanosis, leukocytosis and fever ended in death thirteen days later, following the rapid development of what apparently was congestive heart failure, with rapid enlargement of the liver and pitting edema of the extremities. I think it is fair to say that the heart was probably involved, at least in the last few days. But it is necessary to find another explanation for the previous clinical findings.

On the first admission, there were several things of interest—first of all, the cough and vomiting. I gather that the vomiting soon cleared up following hospital admission, and knowing that vomiting can come from almost anything in an infant, I do not put much stress on that. I think the cough might have had some importance as possibly indicating upper respiratory infection. I shall go in to that a little later.

One of the most interesting findings on the first admission was the rather severe anemia, and in an attempt to explain that, it is necessary to consider several possibilities. Was this a nutritional

anemia? The statement was made in the record that the diet was adequate, and yet physical examination on admission revealed a child who was rather poorly nourished. Did he have an infection that might possibly account for an anemia of this type? The white-cell count was normal. On admission, the temperature was only slightly elevated, and the smear was normal for a patient of his age. Two common causes of anemia in children on an infectious basis are syphilis and tuberculosis. I think we can rule them out by the negative blood Hinton reaction and the negative tuberculin test. The statement was also made that the throat was congested and filled with mucus. Of course, the mucus may have come from the nose or bronchi. The fact that the patient was coughing suggests that it may have come from the bronchi. Coughing was the commonest symptom and occurred fairly soon after the onset of his illness. I doubt if it would have been possible to make a definite diagnosis of bronchopneumonia or lobar pneumonia in this child, but he might possibly have had an upper respiratory infection, even a bronchitis.

Did the patient have pertussis? Whooping cough is very common at this age. He did not have the characteristic paroxysmal cough of pertussis, and yet it is well known that the clinical course is not necessarily classic in pertussis and may fall in a great many different patterns. The fact that the vomiting followed the cough is slightly suggestive. One thing that might be against the diagnosis of pertussis at this particular stage is the absence of a significantly high leukocytosis. It is well known that pertussis gives one of the highest leukocyte responses of any of the upper respiratory infections in children. Of course, it usually does not appear until the paroxysmal stage, but my understanding of it is that it should be present at the end of the second week at least. When the patient was admitted, he had been sick for three weeks.

Then the question arises, Did he have a primary anemia of infancy? One possibility to be considered is sickle-cell anemia. Nothing is said about the race; although sickle-cell anemia occurs almost always in Negroes, it may be seen in Italians.

Can you clear up that point, Dr. Mallory?

DR. TRACY B. MALLORY: The record simply states that the patient was born in Maine. The name suggests Scottish descent.

DR. WILLIAMS: I do not suppose that rules it out. A few features of the illness suggest sickle-cell anemia, which may occur at this age—six months—and apparently gives a picture similar to this, with a color index of almost 1.0, which this child had. Another thing consistent with sickle-cell anemia is the amount of hemolysis, par-

ticularly at the lower range. Hemolysis was not complete until 0.25 per cent. That is frequently seen in sickle-cell anemia. Also, one may see young red forms in the blood smear, which were present in this case. However, there are a few things against this diagnosis. One is the fact that reticulocytes were not mentioned. Ordinarily, there is a very high reticulocytosis with sickle-cell anemia. Another thing is the fact that, although the spleen is not ordinarily felt in adults, I understand that it is felt in children and infants with this disease. A spleen was not felt in this infant at any time. Another thing against it is the absence of icterus, which was not mentioned either clinically or by a laboratory test. Also, I should think that a complete clearing up of the anemia after the first episode would be against sickle-cell anemia. One thing known about the disease is the fact that these patients are susceptible to intercurrent infection. I think we have rather good evidence of infection in this infant. But I am inclined to discard the diagnosis of sickle-cell anemia, especially since we have nothing definite about the racial origin.

One of the other anemias seen in children is Cooley's anemia. There are several things against that. There is no note about the racial origin—Cooley's anemia usually occurs in Mediterraneans. The spleen is always greatly enlarged, and it was not felt in this case. Bone changes that are usually quite characteristic, especially changes in the skull, are not described. Cooley's anemia is likely to show icterus and a low color index, neither of which was found in this patient. The diagnosis of familial hemolytic jaundice can be thrown out, I think, on the absence of family history, splenic enlargement and jaundice. These patients also show decreased resistance to hemolysis by the fragility test, whereas this patient had increased resistance. Von Jasch's syndrome is another possibility. There is supposed to be high leukocytosis along with anemia, with many immature red cells in the blood stream. On admission, the patient had a low leukocytosis, and the blood counts were normal. Moreover, Von Jasch's syndrome, which is not thought to represent any pathologic entity, is simply a pathologic response. Most of the first episode can be explained, I think, by infection, possibly in the trachea, the bronchi or the interstitial tissues of the lung. At this time, there was no definite indication of cardiac abnormality. Examination of the heart was negative. No murmurs were heard, and there was no cyanosis. It is possible that the anemia at the time of admission might have accounted for the absence of cyanosis. However, when the anemia cleared, no cyanosis was mentioned, and I there-

fore assume that cyanosis was not present at that time. The patient did have a rapid pulse, —150,— but in an infant of six months that is not especially exciting. Any slight infection may increase the pulse up that high, so that I think we cannot say very much about the heart.

At the time of the second admission, eight days after discharge, there were several interesting new symptoms. The patient had become dyspneic, something not noticed before, and was definitely cyanotic. This was noticed by the child's mother. At the time of admission, the throat was congested, and there were rales in the lungs. The liver was definitely enlarged. Also, the blood findings were interesting because of the high leukocytosis with only 55 per cent polymorphonuclears. I find that a little hard to explain, but the fact that the next day the white-cell count had subsided to 18,000 with a much higher percentage of polymorphonuclears is a little more comforting and quite consistent with infection. The pulse, which was 160 to 170, was likewise consistent with infection. I think one of the most interesting facts was that, although the physical signs pointed to congestion and possibly consolidation of the lungs, the heart sounds were normal on physical examination, and no murmurs were heard. Ordinarily, with congestion of the lungs on the basis of cardiac failure, the x-ray picture shows cardiac enlargement, and almost invariably a murmur is heard. All this suggests that something in the lung might account for the symptoms and that the heart was not yet involved.

The statement was made in the x-ray report that the heart was normal in size and configuration. The mediastinum was apparently displaced somewhat to the left, but without shift on respiration. At fluoroscopy, there was no definite consolidation. I wonder if the patient could have had bronchopneumonia. Frequently, in bronchopneumonia, the x-ray picture is not too clear cut.

DR. MALLORY: We had the x-ray men review these plates, and they were unable to find any abnormality in the lung fields.

DR. WILLIAMS: There was nothing to account for rales. It has been said that bronchopneumonia of the interstitial type may produce definite signs on physical examination without showing much by x-ray examination. I hope that was so in this case. At any rate, bronchopneumonia in infants is a very common cause of cyanosis, especially if it has been present for some time. I had hoped to explain the cyanosis on the basis of bronchopneumonia.

How can we explain the terminal cardiac failure and possibly the cyanosis, if bronchopneumonia is out? First of all, rheumatic heart disease seems

extremely unlikely at this age, although it may have been reported in infants this young. The electrocardiogram showed a sinoauricular tachycardia, with a rate of 150, and a PR interval of 0.12 second, which is within normal limits for this age and heart rate. I consider rheumatic heart disease not very likely. If the patient had congenital heart disease, I find it difficult to make any single diagnosis. The absence of enlargement by x-ray and murmurs rules out a great many of the congenital heart lesions. I should say that this included primary idiopathic hypertrophy, interauricular septal defects, interventricular septal defects, patent ductus and other conditions. Ordinarily, most of these do not end in death at this early age, unless attended by some complication. I think that covers the group without cyanosis or with primary cyanosis. Then, in the moderate to extremely cyanotic group, I think the tetralogy of Fallot, pulmonary atresia with transposition of the great vessels and other lesions are quite well ruled out by the absence of cyanosis at birth and of significant x-ray findings. However, one congenital defect that should be considered is origin of the left coronary artery from the pulmonary artery, which may give a picture consistent with this patient's story. The characteristics of this condition are freedom from symptoms during early weeks of life, with death usually occurring during the first year, and the prominent symptoms are cyanosis, dyspnea and sometimes chest pain, occasionally a peculiar kind of sweating, in which the infant sweats for no reason. That was seen in this case, but there may have been another reason for it. One thing very much against this diagnosis is the fact that in all the 8 cases in a series reported by White, Bland and Garland* the heart was enlarged for some time before death. That was not true in this patient. Also, in the cases in which an electrocardiogram was obtained, T wave changes were observed. Nothing was said about the T waves in this electrocardiogram.

DR PAUL D. WHITE: Let me read the three electrocardiographic reports taken a few days apart, with Dr Porter's opinions.

Sinoauricular tachycardia, rate 150, PR interval of 0.12 second, moderate right axis deviation. The record indicates right ventricular strain, which suggests a congenital lesion or acute ventricular failure.

Sinoauricular tachycardia, rate 155, PR interval of 0.12 second, moderate right axis deviation, slight inversion of T₃. No significant change from the last record.

Sinoauricular tachycardia, rate 150, moderate right axis deviation, inverted T₃. No significant change from the last record.

*White P. D., Bland E. P. and Garland J.: Congenital anomaly of coronary artery: report of unusual case associated with cardiac hypertrophy. *Am. Heart J.* 8: 87-92, 1933.

DR WILLIAMS: I should think those findings would be against the diagnosis of origin of the left coronary artery from the pulmonary artery, which of course produces myocardial degeneration and hypertrophy, as well as electrocardiographic changes that are diagnostic.

Did this patient have endocarditis? There is nothing to support that diagnosis. The absence of murmurs, petechiae and so forth, as well as the absence—so far as one can tell—of an underlying valvular lesion, would be against it. One other thing that might explain the terminal failure is acute nephritis. It is well known that, in infants and young children, heart failure may follow acute nephritis without hypertension or without nitrogen retention. The one nonprotein nitrogen reported was normal. I presume that was done at the time of admission. It is possible that this patient had nitrogen retention later. Nothing is said about subsequent urines.

DR MALLORY: A second urinary examination ten days after the first was entirely negative.

DR WILLIAMS: Was that at the time of the first admission?

DR MALLORY: At the second admission.

DR WILLIAMS: That seems to throw out nephritis. Another disturbing point against the diagnosis of nephritis is the fact that there was no anemia during the second admission. Anemia is almost invariably present in acute nephritis in children. I wonder if some pulmonary lesion accounted for the cyanosis and produced secondary polycythemia and thus offset an anemia based on nephritis. Nephritis would also explain the acidosis, which may possibly have been due to a pulmonary lesion, however.

The electrocardiogram is not very much help at this age. One may see right axis deviation at six months of age in normal infants, but the axis is usually normal at this age.

When I read this over, my final diagnosis was question of bronchopneumonia, possibly following pertussis, with acute nephritis and cardiac failure. The negative urine findings are a bit upsetting, but I do not know how to explain the terminal cardiac failure otherwise because I cannot find, from the data given, any good evidence for a structural change or a congenital lesion that might account for it, accordingly, I shall have to leave it at that.

DR WHITE: Do you not believe Dr Porter paid more attention to the possibility of abnormality in the electrocardiogram? As noted in his very first statement, he was apparently impressed by the fact that there was a moderate degree of right axis deviation, and he said that later records showed

the same deviation. Did it suggest a congenital defect or right ventricular strain beyond what was expected at this age of six months? I think that may be of considerable importance.

DR. WILLIAMS: One thing I wondered was whether, at the time the electrocardiogram was taken, the patient already had enough acute right-sided failure to account for right-axis deviation. I found it very hard to account for on the basis of the usual things, such as pulmonary stenosis, the tetralogy of Fallot and conditions commonly known to produce right-axis deviation. I can see no evidence for acute cor pulmonale on any basis.

DR. WHITE: It is interesting that in the first year of life congenital heart defects cannot be ruled out readily and may be diagnosable only at a later date. I do not know what this youngster had, but the possibility remains that a congenital heart defect was present and did not show up until six months or more after birth, with the delayed appearance of clubbing and cyanosis and with more electrocardiographic right-axis deviation than usual.

DR. WILLIAMS: The clubbing was disturbing. I wondered if it was due to pulmonary involvement, which would also explain the heart failure. When these other things were fitted together, it left the field wide open. If there were a tetralogy of Fallot, it should give changes by x-ray examination. Could the terminal cyanosis have been due to auricular septal defect? One would then have a better explanation for the electrocardiogram without having to relate it to immediate strain and failure from other cause. Can one make a diagnosis of the tetralogy of Fallot in the absence of murmurs?

DR. WHITE: I think so, although I should hesitate, as in this case, to make the diagnosis of a structural cardiac defect during the first year of life without more proof, although such a condition should be considered possible.

DR. MARGARET M. GLENDY: There was one clinically interesting observation not brought out in the abstract. The child was admitted on Saturday afternoon. On Sunday morning, there were fine rales in the lungs, and the liver was only 3 cm. down. On Monday, it was down to the crest of the ilium. The cyanosis was present from the time of admission until death.

DR. WILLIAMS: I thought the rapid liver enlargement ought to be explained by progressive right-sided heart failure, but again the field is wide open.

DR. WHITE: There is only one x-ray report. The heart shadow might have become greatly enlarged before death and might have changed sig-

nificantly, as with the development of a pericardial effusion that might have caused a terminal tamponade.

DR. MALLORY: Dr. Edward F. Bland saw this case in consultation and made the following note:

I agree with the observations of others. Today, the patient is slightly cyanotic even in the oxygen tent. I hear no murmurs or gallop. In view of the cyanosis, the right-axis deviation and the globular-shaped heart by x-ray, I think he has congenital heart disease—probably a combination of defects, with patency of the septum (auricular) and possibly of the ductus as most likely. The prognosis is probably unfavorable.

He was at least correct in the last statement.

CLINICAL DIAGNOSES

Congenital heart disease.
Cardiac failure.

DR. WILLIAMS'S DIAGNOSES

Cardiac failure, right-sided.
Bronchopneumonia.
Acute nephritis.

ANATOMICAL DIAGNOSES

Congenital alveolar atelectasis.
Pulmonary arteriolar hypertrophy.
Cor pulmonale.
Chronic passive congestion of systemic circulation.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Post-mortem examination showed a somewhat enlarged heart, with marked hypertrophy of the right ventricle. The right ventricle measured 5 mm. in thickness, which, even in an adult, is probable evidence of cor pulmonale. In an infant, it is an extreme degree. The left ventricle measured 6 mm. The lungs at the time of autopsy seemed reasonably well distended and aerated, although they were just a little subcrepitant. They were not edematous. It was obvious that there was cor pulmonale, for which there was no gross anatomical explanation.

On microscopic examination of the lungs, two things were obvious. The small pulmonary arteries were considerably thicker than normal. In fact, they looked like systemic, not like pulmonary, vessels. This thickening was due to true hypertrophy, primarily of the muscular layer of the wall. There was no endarteritis and no evidence of narrowing of the lumens, so that one must assume that pulmonary hypertension existed without primary vascular disease to explain it. Dr. Ronald C. Sniffen studied these vessels with

considerable care, measuring their internal and external diameters and calculating their ratios. The results from this case, from a similar one in another infant and from those of two control patients of the same age appear in Table 1. Three

TABLE 1. Ratios of External Diameter to Lumen Diameter

CASE	EXTERNAL DIAMETER OF VESSELS		
	600-1200 μ	450-550 μ	200-400 μ
Present case	18	25	24
Similar case	18	33	21
Control 1	13	14	15
Control 2	12	13	15

ranges of arterial size were studied in each case. The greatly increased thickness of the arterial walls, particularly in the smaller sizes of arterioles, is clearly brought out.

The lung parenchyma proved interesting in that there were practically no expanded alveoli and yet grossly the lung was not atelectatic. All the alveolar ducts and small bronchioles were grossly overexpanded so that the total amount of air in the alveoli was not much below normal. That is a very unusual form of atelectasis. It was uniform in all parts of all lobes. Ordinarily, with atelectasis, the alveolar ducts are collapsed, as well as the alveoli in the areas involved. Here the ducts were everywhere overdistended. In the collapsed alveoli, there were many accumulations of desquamated septal cells, which looked as if they had been present for a long time—I know of no way of estimating how long, but I am quite sure far longer than the duration of the final illness. It seems to me not impossible that this may even have gone back to birth and the patient had lived all these months ventilating only with his respiratory bronchioles. In any child dying a few days after birth, it is not uncommon to find large areas of lung tissue in which the alveoli have not expanded, and yet these lungs will transilluminate by x-ray in normal fashion.

DR WHITE: Is that the cause of death in these cases?

DR MALLORY: No; it is not. These children are not cyanotic, since some time can elapse before the child needs all his lung tissue to keep the blood oxygenized. The pediatricians may dispute this point, but I think Dr Sidney Farber would agree. I have seen one other case, which is identical, in a child of approximately the same age, but unfortunately, the clinical history was inadequate. It showed the same hypertrophy of all the pulmonary arteries and the same failure of expansion of alveoli, and I am strongly tempted to tie the two together. I think that the lack of expansion of alveoli is in some way responsible for pulmonary

hypertension and that the arterial changes are secondary. Dr. Williams's suspicion that the cardiac picture was in some way secondary to the pulmonary lesions is entirely correct.

DR WHITE: Has this clinical entity or syndrome been described yet, and are you going to put these two cases together?

DR MALLORY: I wish I knew more about the other case. We had only the heart and lungs, without any clinical findings to go with them.

DR WHITE: Was there any evidence of infection in this case?

DR MALLORY: No; we did find, in the myocardium, a few foci of lymphocytes. I suppose one could speak of myocarditis, although not enough to be of importance. I am sure there was no rheumatic fever.

DR WHITE: Was there acute right ventricular failure?

DR MALLORY: Yes

CASE 28402

PRESENTATION OF CASE

A fifty nine year-old Irish American unemployed man was admitted to the hospital because of pain in the lower abdomen and flanks.

Five months before entry, the patient was operated on in a community hospital for repair of bilateral inguinal hernias. He was discharged after an uneventful postoperative course of twenty-one days. After this, he experienced almost constant soreness and tenderness in the lower abdomen and flanks. He also had sufficient headache to keep him awake at night. About three months before entry, he had an attack of fever, for which his physician put him to bed for a week, with a special diet. The soreness and tenderness in the abdomen and flanks persisted. About a month later, a long dark blood clot was passed in the urine. Subsequently, several similar clots were passed. There were no other urinary complaints, and only occasional nocturia. There was a loss of about 18 pounds of weight during the illness.

The patient admitted the use of much beer and wine. The past history was otherwise irrelevant.

On admission, the patient appeared pale and thin. The tongue was beefy red and dry. The lungs seemed emphysematous. The heart was slightly enlarged to the left, with a moderately loud systolic murmur at the apex. Bilateral scars of recent herniorrhaphies were present. Both kidneys were palpable; the right was ballotable and down four to six fingerbreadths below the costal margin, whereas the left was down about one fingerbreadth. The costovertebral angles were

tender. The prostate felt firm and rubbery, and was of normal size. There was slight hypospadias of the glans.

The blood pressure was 140 systolic, 80 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 3,900,000 with 75 per cent hemoglobin, and a white-cell count of 14,500 with 76 per cent polymorphonuclears. The blood Hinton reaction was negative. The urine showed a specific gravity of 1.012, a +++ test for albumin, and many red cells and a few white cells in the sediment. The urine culture showed abundant growth of colon bacilli. The blood nonprotein nitrogen was 30 mg. per 100 cc.; the chloride was 97.5 milliequiv., and the bicarbonate 25.2 milliequiv. per liter; and the serum protein was 6.7 gm., the calcium 10.3 mg. and the phosphorus 7.0 mg. per 100 cc.

A roentgenogram of the chest showed multiple adhesions of the diaphragm and thickening of the pleura on the left side. The heart was slightly enlarged in the region of the left ventricle, and the aorta was tortuous, elongated and calcified. A flat film of the abdomen showed a clear psoas shadow on the right, and diminution in visibility of the shadow on the left. The right kidney shadow was obscured.

An intravenous pyelogram, taken in the Out Patient Department shortly before admission to the hospital, showed the right kidney outline to be indistinct and unusually large. The left was slightly larger than usual but of normal shape. An area of calcification overlay the upper pole of each kidney, consistent with costal cartilage. The left kidney showed normal excretion of dye and normal contour. The bladder appeared small. Both sacroiliac joints were fused.

On the day after admission, retrograde pyelography was attempted, without success. A roentgenogram showed the catheters to have extended to both renal pelves. The shadow of the right kidney seemed large.

Following cystoscopy and ureteral catheterization, the patient remained anuric for about twenty hours. The blood nonprotein nitrogen rose to 67 mg. per 100 cc. The temperature spiked to 103°F. for a few days, and then varied from 98 to 100°F. for the next two weeks. Urine gradually reappeared, but the output remained low. The urine was not bloody. There were occasional vomiting and nosebleeds. A blood culture grew colon bacilli in both flasks. For the first five days, the patient was given a daily intravenous infusion of 1500 cc. of 10 per cent glucose in physiologic saline solution.

The patient failed to improve. Although the urinary output increased satisfactorily, the nonprotein nitrogen of the blood rose to 158 mg. per 100 cc., and the chloride to 113 milliequiv. per liter; the bicarbonate fell to 17.0 milliequiv. per liter, and the protein to 5.1 gm. per 100 cc. The patient was therefore transfused in an attempt to raise the serum protein and improve kidney function. On the twenty-third hospital day, the temperature again began to spike, reaching 105°F. In the next week, the patient continued to do poorly. He complained of chest pain and was intermittently irrational. Slight dependent edema appeared. The urinary output continued fair, and the blood nonprotein nitrogen dropped to 97 mg. per 100 cc. Terminally, rales were heard in the chest, and Cheyne-Stokes respirations set in. Death occurred on the twenty-seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. J. DELLINGER BARNEY: "Both kidneys were palpable; the right was ballotable and down four to six fingerbreadths below the costal margin." That may mean they were palpable because they were large or merely that they were low.

The tender costovertebral angles indicate an infectious process in or around the kidneys.

The blood studies show a certain degree of secondary anemia, and a moderate leukocytosis.

One would have to think of the possibility of nephritis or a polycystic kidney, and of tuberculous kidney or a bilateral tuberculosis. Tuberculosis can perhaps be excluded, because we generally get a sterile urine with tuberculosis. In this case, there were colon bacilli in the urine, and no instruments had been passed, so that there was no chance for external infection.

The very high phosphorus suggests uremia.

The right kidney shadow was obscured but apparently large on each of several examinations. I should like to know if the outline, so far as it could be seen, was regular or had lobules suggesting cysts, multiple or solitary, or neoplasm. We know more about the left kidney from the record than we do about the right. The left kidney showed normal excretion of dye and normal contour. Nothing is said about the right side.

DR. TRACY B. MALLORY: I think it is safe to assume that there was no excretion on the right side.

DR. BARNEY: If they succeeded in getting the catheters up to the renal pelves, I should like to know why they were unsuccessful in injecting dye into them.

From the story, one can safely say that the patient had a cystoscopy reaction, which is not very common but does occur. Although, under certain

itions, such a reaction might be considered avoidable, we must remember that at least one hologic kidney was present.

do not know that I can explain the nosebleeds, the vomiting may have been due to renal insufficiency. The high blood phosphorus and the high nonprotein nitrogen are confirmatory evidence. The patient had a colon-bacillus blood-stain infection, which might well have resulted in a primary renal infection. Intravenous infusion of glucose was given in an effort to overcome this infection and the anuria by re-establishing proper excretion of urine. Nevertheless, the nonprotein nitrogen climbed to 158 mg. per 100 cc. indicating that the process in the kidney was initially worse.

So far as the final episode is concerned, one must think of pneumonia, infarct of the lung and possibly, pulmonary embolism.

Without going into all the details of this case, it seems to me that this man was well until after his hernias were repaired. He then began to get a little trouble. We do not know about the past history. Apparently, it was irrelevant. The patient had not had this trouble before. When he came to the hospital, it was found for the first time that he had certainly low and certainly enlarged kidneys. The costovertebral angles on each side were tender, and there was some infection, as shown by a certain amount of pus in the urine and the growth of colon bacilli from the urine. I should say that this kidney process involved particularly the right side, was of long standing and, after the hernia operation, flared up. The patient was cystoscoped, catheterized and so on, which made the matter still worse, and the kidney function fell off quite markedly. The infection in both kidneys continued, however, and he developed a generalized colon-bacillus infection.

The question is, What process would involve both kidneys and give a picture like this? We must consider a variety of things, particularly bilateral polycystic kidneys, in spite of the pyelogram. On one side, there was apparently normal excretion, and on the right side,—with the larger kidney,—there was no excretion of dye at all. I think polycystic kidney is not incompatible with the finding of a nonprotein nitrogen of 30 mg. or 100 cc. when the patient first came in. The left kidney might be doing enough work to compensate for the right kidney to a large extent, but not entirely. On the other hand, polycystic kidneys in a man of this age—fifty-nine—are unusual. Such patients often die earlier, and they generally have a previous history of hematuria, pain and infection.

But that would account for a good deal of the picture. Again, this may have been a simple cyst, but I do not believe such a cyst would put one kidney out of action.

Tumor must be considered. Again, new growth involving both kidneys is extremely rare. Tuberculosis, I think, can be ruled out because of the lack of symptoms, although there was evidence of old trouble in the chest, but not the symptoms one usually sees with renal tuberculosis, such as bladder irritability, and colon-bacillus infection is unusual with tuberculosis.

We must also consider pyonephrosis, with extensively damaged and infected kidneys. I think that there would have been a great deal more pus in the urine with such a condition and that, during some time before cystoscopy was performed, the patient would have had a higher temperature and more pain than is recorded. The possibility of lymphoma must not be forgotten. It might, in some bizarre way, involve both kidneys and perhaps give the picture that we have.

It is difficult to evaluate all the symptoms and put them together, but my first diagnosis is polycystic congenital kidneys.

DR. MALLORY: Would you like to see the x-ray films before you commit yourself?

DR. LAURENCE L. ROBBINS: This simply shows the large right kidney; the left kidney, so far as I can determine, is normal in size and shape and excretes the dye normally.

DR. BARNEY: The left kidney may, as you say, excrete the dye normally so far as it excretes it, but there is very little dye. There is no evidence whatever of pelvis or calyces on the right side. I believe that the kidney was extensively damaged. On that basis alone, it seems to me that a polycystic kidney can almost be ruled out. I think one can also rule out the possibility of tuberculosis, as well as nephrosis and pyonephrosis.

I cannot say anything better than polycystic kidney.

DR. WILLIAM B. BREED: You ruled out everything, did you not, Dr. Barney?

DR. BARNEY: Nearly.

DR. WILLIAM C. QUINBY: I should like to know why they could not make a pyelogram. They put the catheter high up. The point is just here, gentlemen: the outstanding assets of the urologist's diagnostic armamentarium are the cystoscope and the ability to make pyelograms by injecting opaque fluid through a ureteral catheter; if one does not do it and if one cannot give a reason why it was not done, the whole discussion is reduced

to a guessing match because no one would try to make a diagnosis without that evidence.

DR. MALLORY: I think, Dr. Quinby, that is merely putting the genitourinary surgeon on a par with the medical man. It is only fair once in a while to ask him to guess too, because the medical man is rarely able to visualize the pathologic lesions that he must diagnose.

DR. QUINBY: True enough, but if there is a direct way of making a pyelogram, why not do it? A medical man is not expected to make a diagnosis of cardiac lesions without an electrocardiogram.

DR. BREED: Is there some explanatory note, or is the person here who did the cystoscopy?

DR. MALLORY: No; but I assume that the patient was quite ill and, possibly, had some sort of reaction on the table, and they believed they could not continue.

DR. BARNEY: The retrograde pyelogram was unsuccessful. That is all we have to go by in the record.

CLINICAL DIAGNOSES

Bilateral pyelonephritis.

Pyonephrosis?

Uremia.

Bronchopneumonia.

Coronary heart disease.

Renal tumor?

DR. BARNEY'S DIAGNOSIS

Polycystic kidneys.

ANATOMICAL DIAGNOSES

Renal-cell carcinoma (hypernephroma type) of right kidney, with extension along renal vein into vena cava and with metastases to splenic vein.

Pyelonephritis, acute and chronic, left kidney.
Bacterial endocarditis, colon bacillus, aortic valve.
Cerebral infarct, septic.

Pleuritis, chronic fibrous, bilateral.

Operative scars: herniorrhaphy, bilateral.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At autopsy, we found an extremely large kidney on the right, which was filled with tumor, a characteristic hypernephroma. In typical fashion, the tumor had grown up the renal vein, and a plug of tumor tissue protruded into the vena cava for a distance of 3 cm. This tumor thrombus in the cava was not large enough to cause obstruction, although, occasionally, real caval obstruction is produced in this way. An unusual and unexpected finding was a solitary metastasis in the splenic vein, which was completely occluded by the tumor. The other kidney showed a fairly severe pyelonephritis.

There was also a terminal bacterial endocarditis due to colon bacillus, — it will be recalled that the blood culture was positive, — and an embolus from the vegetation on the aortic valve had produced a small area of softening in the brain. There were old pleuritis and healed tuberculosis of the lungs, but no pulmonary metastases.

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COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

INSTRUCTION IN INDUSTRIAL MEDICINE

THE joint announcement of the Committees on Postgraduate Instruction and Industrial Health of the Massachusetts Medical Society in this issue of the *Journal* is a local expression of the widespread and growing consciousness of the importance of health in industry. This is not entirely a medical awakening. While the medical profession, whose general interest has always been the preservation of health, is striving to orient itself, the industrialists, whose primary interest has heretofore been costs, production and quality of output, are likewise showing an appreciation of the

potential value of a physiologically sound employee.

Evidence of the interest of Massachusetts manufacturers is found in the current issue of *Industry*, the official organ of the Associated Industries of Massachusetts, where a series of twelve excellent and appropriate articles dealing with the health of workers is appearing. It is a safe prediction that before the passage of another year more than one physician in Massachusetts will be asked by an employer or personnel officer to give an opinion or discuss a problem that was suggested by one of this series of articles. The progressive physician should prepare himself.

Throughout the United States, the vital significance of industrial medicine has been recognized. Iowa has organized and presented an institute on industrial health; at Yale University, a series of ten weekly exercises will be given this fall; in Brooklyn, an intensive two week course has been announced, and so it goes. Alive and alert to all this, the Council on Industrial Health of the American Medical Association is keeping abreast, and serving in a particularly useful way by disseminating information from one part of the Nation to another.

The announcement referred to above asks that interested physicians mark November 7 on their calendars. Every doctor who is called into the manufacturing plants of his locality—especially into the smaller plants, and even though he is called but rarely—is an “interested physician,” and the role he plays may be exceedingly vital. It is now plain that the war is to be won or lost by a narrow margin, and this is a critical period in the battle of production.

LEGAL ASPECTS OF FIRST AID

A LETTER¹ in a recent issue of the *Journal* called attention to a situation that needs to be clarified. Will the lay persons who administer first aid run the risk of becoming defendants in lawsuits brought by dissatisfied victims of bombing or other disaster? No specific legislation has yet been passed, and any opinion advanced must be accepted

for what it is worth — that is, as a mere expression of belief regarding what the probable outcome of such lawsuits would be.

In the first place, it should be pointed out that those who administer first aid are liable to litigation, since "any aggrieved person, with or without cause, can file an action at law."² The validity of the suits will be decided by courts of law. Until the merits of such claims in the imminent, unprecedented circumstances have been assessed by the courts, it is reasonable to assume that the principles involved would be analogous to those in suits for malpractice brought against physicians.

A recent study³ of the problem poses several questions and attempts to give answers, which are admittedly not applicable universally. The first-aid worker would be reasonably protected if he followed rules accepted by the American Red Cross and the civilian-defense groups throughout the Nation. The necessary skill and precaution are defined as "such care as a reasonably prudent person should exercise, considering all the circumstances such as the injury itself, the entire situation of the emergency, [and] the training of the first aider." The authors' statement that those trained in first aid are probably under a legal duty to render such care seems unwarranted in view of the following statement by a recognized legal authority⁴: "No duty rests on a physician to accept an employment. He may refuse arbitrarily to engage his services." If a physician is not required by law to treat a patient, how can a different rule be applied to a first-aid worker?

Presumably, the layman trained in first aid has no more responsibility and is entitled to no less protection than the physician. Accordingly, the defense of the latter against litigation should apply equally to the former. And the specialist in legal medicine referred to above has this to say concerning the results of treatment, "A physician is not a guarantor either of his diagnosis or of his treatment, and the required negligence necessary for his liability is not made out by mere evidence of results of treatment or a failure to cure or a disappointing result."

Although it must again be emphasized that the layman's risk cannot be specifically assessed at present, it is apparent that anyone who follows conscientiously the accepted routine of first-aid treatment is in little danger of being successfully sued by the aggrieved recipient of his ministrations. Laws are passed to deal with situations that arise, and court decisions are based on the law, on precedent and on the human factors involved. Those who attempt to relieve suffering and save lives should have no fear that justice will tolerate unwarranted claims against them. Nevertheless, there is urgent need for statutes defining the rights and duties of civil-defense workers. These should be put into effect now — before the evil emergency is upon us.

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MEDICAL EPONYM

ROENTGEN RAY

The discovery of the x-ray was announced at a meeting of the Physico-Medical Society in Würzburg in 1895. The paper by Wilhelm Conrad Roentgen (1845-1923), "Über eine neue Art von Strahlen (On a New Kind of Rays)," appeared in the *Sitzungsberichten der Würzburger physikalisch-medizinischen Gesellschaft* (1895, pp. 132-141). A portion of the translation follows:

If in a completely darkened room, one allows the discharges from a large Ruhmkorff coil to pass through a Hittorf vacuum tube (or a sufficiently evacuated Lenard's, Crookes's or other similar apparatus) and covers the tube with a rather closely fitting jacket made of thin black cardboard, a paper screen which has been painted with barium platinum cyanide will be seen to glow brightly and become fluorescent when brought near the apparatus. It makes no difference whether the painted or the unpainted side of the screen is turned toward the source of the discharge. . . . In the presence of this phenomenon one is first struck by the fact that some agent is passing through the black cardboard jacket — a jacket which will not allow the passage of either the visible or ultra-violet rays of the sun or the rays of an electric arc light; further, that this agent is able to generate a marked fluorescence. . . . It will be found that all bodies

are permeable to this agent, but in very different degrees. Paper is very permeable. Thick blocks of wood are also permeable. Sheets of hard rubber several centimeters in thickness still permit the rays* to pass through.

*For the sake of conciseness I should like to use the expression rays, and to distinguish them from others the name x rays

R. W. B

MASSACHUSETTS MEDICAL SOCIETY

AMERICAN MEDICAL ASSOCIATION

After prolonged and intensive consideration, the Board of Trustees of the American Medical Association has come to the conclusion that the annual session of the association scheduled to be held in San Francisco in 1943 should be canceled. An official meeting of the House of Delegates will be held in Chicago at a time to be announced.

COMMITTEES ON POSTGRADUATE INSTRUCTION AND INDUSTRIAL HEALTH

On August 17, the Committee on Industrial Health voted to hold a comprehensive one-day program on industrial medicine, to be organized with the interests of general practitioners and part time industrial physicians in mind, and to be held, if possible, in co-operation with the Committee on Postgraduate Instruction. The two committees met in joint session on September 2, and are now collaborating on a program to be held on Saturday, November 7, morning, afternoon and evening, at the Harvard Club in Boston. The subjects to be discussed, the speakers and the dining and registration arrangements will be announced within a few weeks. Interested physicians are asked to mark the date on their calendars.

REGINALD FITZ, *Chairman*
Committee on Postgraduate Instruction

DWIGHT O'HARA, *Chairman*
Committee on Industrial Health

COMMITTEE ON MATERNAL WELFARE*

CASE HISTORY POST PARTUM HEMORRHAGE,
FOLLOWED BY CEREBRAL HEMORRHAGE AND DEATH

A thirty five year old primipara at term had been seen routinely during a normal pregnancy. The past history was entirely irrelevant. She was delivered by low forceps, labor consuming eight

*Beginning with the October 15 issue of the *Journal* a resume of the maternal mortality in Massachusetts for the year 1941 will appear. It is planned to present an exhaustive analysis of this investigation. An article to be published each week for some time.

hours and being complicated in no way. The placenta was delivered spontaneously, and there was no hemorrhage. The blood pressure during labor was 90 systolic, 60 diastolic. The day following delivery, the patient developed a severe headache, and the blood pressure rose to 160 systolic, 90 diastolic. There was no note of convulsions. Hemiplegia developed soon after the onset of the headache, and death occurred three days later. Autopsy showed cerebral hemorrhage (basal ganglion and right internal capsule), subacute nephritis and fatty degeneration of the liver.

Comment. It is fortunate that an autopsy was performed, for the subacute nephritis and fatty degeneration of the liver are suggestive of a fulminating toxemia post partum as the basic cause of death. From the headache and increased blood pressure one might have inferred that an unusual post partum toxemia was responsible, but without the autopsy, the clinical diagnosis of cerebral hemorrhage would probably have been made. The value of the autopsy in this case illustrates how helpful it would be if autopsies were more frequently performed.

WAR ACTIVITIES

CIVILIAN DEFENSE

At a meeting of various members of the Medical Division, Massachusetts Committee on Public Safety, held at the Parker House, Boston, on August 26, the following matters were emphasized by Dr. A. William Reggio, the medical director:

1. Changes have been advised regarding the setup of medical first aid posts so that they may function more easily in conjunction with local conditions. It is suggested that the number of first aid posts in all communities be divided into first line active and second line reserve posts, that is, one half on the active list and the other half on the reserve list, because of the increasing shortage of physicians. It is also believed that if half the number of posts are active, well drilled, and completely manned and equipped, they can cope with almost any situation that may arise. This in no way should upset the present setup or disturb the work that has been done. It is merely a way of improving the setups and of somewhat lessening the strain on each community. It is also suggested that members of the dental profession be used more in these mobile posts, and in those communities where there are well trained veterinarians that they could also be utilized, with a little instruction. Practice sessions for these first line mobile posts are urgently recommended. In this way, it is also believed that a spirit of competition will arise as a result of which the second line reserve posts will feel a greater incentive to graduate from the reserve to the active list.

2. In those communities where emergency hospitals are established, at least one first aid post must operate from such a hospital. This in no way should upset the present setup in any community. It is merely an ad-

junct to the already existing posts and is a requirement laid down by the United States Office of Civilian Defense in Washington.

3. Before long, the regional medical heads will receive a number of certificates to be given to all members of the Medical Division already enrolled in the Massachusetts Committee on Public Safety. These certificates show evidence of the fact that the holder has been enrolled as a member of the United States Citizens' Defense Corps. The holding of such a certificate by each member is essential. The reason is that government supplies are now being allocated and will be distributed only to those communities in which every member of the Medical Division has been so enrolled. This in no way changes the status or allegiance to the state organization but is merely additional evidence of the fact that all members are also enrolled in the United States Citizens' Defense Corps as the second line to the Army and Navy.

4. The question of nonmedical deputies being appointed to sit and function in the report centers in some localities has been raised. It seems advisable to plan on this, owing again to the increasing scarcity of physicians. If such a nonmedical deputy is appointed, it is essential that the medical director's office be notified of his name, address and telephone number.

5. Since the Massachusetts terminology of medical setups differs somewhat from that used in the Office of Civilian Defense, a listing of the equivalent terms should help to avoid confusion in future communications. These are as follows:

MASSACHUSETTS	OFFICE OF CIVILIAN DEFENSE
Report center	Control center
Base hospital	Emergency base hospital
Emergency hospital	Casualty receiving hospital
Medical first-aid post	Mobile medical or Emergency Medical Service teams (2)
Stretcher bearers	Stretcher teams
First-aid party	First-aid squad
Chief medical officer	Local chief of Emergency Medical Service

CORRESPONDENCE

DEPRIVATION OF LICENSES

To the Editor: At a meeting of the Board of Registration in Medicine held September 16, the Board voted to suspend the license of Dr. Leo Leinwald, 1218 Commonwealth Avenue, Boston, because of gross professional misconduct in the practice of his profession as shown by false evidence in a court case.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

To the Editor: At a meeting of the Board of Registration in Medicine held September 16, the Board voted to find Dr. Zarch, 32 Prospect Street, Bridgewater, guilty of deceit in filing his application for the examination in November, 1941, and voted that his license to practice medicine in the Commonwealth be revoked and action suspended.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

REPORTS OF MEETINGS

BOSTON CITY HOSPITAL.

The fourth in the series of lectures on war medicine, sponsored by the Boston City Hospital House Officers' Association, was held at the hospital on May 14.

Dr. Maxwell Finland discussed "Communicable Respiratory Diseases in Wartime." It was emphasized that the streptococcus, although the commonest offender of the group, owes its importance largely to complications of the original infection. This has become especially true since the widespread use of the sulfonamide compounds.

Since World War I, but more especially in the early stages of the present war, many advances have been made in the understanding of these complications. The most significant observation is that the secondary invaders are usually a different type of streptococcus, especially in complications that occur later than ten days. They are really cross-infections, and should be so treated. Otitis media is still the commonest sequela. Prevention may be attempted by proper segregation according to types of organism, but even this is not entirely satisfactory.

The question always arises, When may scarlet fever be said to exist or to be epidemic? All the Group A streptococci are toxigenic to some extent, and whether a person will have the signs of tonsillitis or scarlet fever depends on the balance between the virulence of the organism and the resistance of the host. Therefore, there is always some scarlatina during streptococcal epidemics, and the same type of organism has been identified in the two kinds of manifestations of the same epidemic. The fact that the organisms causing the current cases of scarlet fever are of low toxicity will probably lead to more recurrences, for the formation of antibodies in such cases is poor. Such patients may remain positive to the Dick test and may fall prey to even slightly more potent streptococci. Recurrences have been reported in as high as 8 per cent of some epidemics.

Rheumatic fever is becoming more generally recognized as a definite sequela of streptococcal infections. But it is necessary to have a susceptible host and a certain unknown characteristic of the organisms to activate the process. Family background apparently plays a role. The incidence of complications in rheumatic fever is higher than physicians generally realize, especially if one observes the patient over a sufficiently long period with adequate tests.

Measles is the next most important communicable disease in army camps, largely because this supposedly innocuous exanthematous condition becomes more serious in such congregations of conglomerate groups of men. Epidemics occur invariably after a large influx of new men who are tired from the rigorous new life and are largely or partly from rural districts where measles has not been encountered. The seriousness of such epidemics is proportional to the number and severity of secondary infections. The streptococcus, which is the commonest secondary invader, attacks a respiratory tract whose entire length has been prepared by the preceding virus. Serious streptococcal pneumonias may be aborted by the proper use of chemotherapy, which should check the spread of virulent streptococci both in the individual respiratory tract and from person to person.

Influenza, it has been demonstrated, may be widespread without much disability or mortality, but a second wave, with its fearful secondary pneumonias, may be catastrophic. If the secondary invader is the pneumococcus, the prognosis is that of any well-treated lobar pneumonia, and the disease should not be serious since the ad-

of chemotherapy and the improvements in specific serum. In infections with the hemolytic streptococcus, which is the complicating organism following throat measles epidemics, the prognosis is not so favorable as with the sulfonamide drugs. But by far the most promising prospect is the widespread pulmonary necrosis that follows staphylococcal invasion and gives every indication of being not only more prevalent but less amenable to even the best forms of chemotherapy.

Lobar pneumonia is the most hopeful of all the communicable respiratory diseases since the advance of chemotherapy and serotherapy. The new fad of calling typical cases virus pneumonias is deprecated. Certain viruses are known to produce such pneumonitis particularly psittacosis and influenza but the last is the only common one. Most cases of influenza are now considered to be due to virus, since comparable syndromes are observed in the ferret, with widespread pathological changes and no bacteria. By proper culture methods *aemophilus influenzae* can be demonstrated in the respiratory tracts of most people who are well or suffering from mild upper respiratory infections. Therefore this is very likely only a secondary invader.

The prevention of communicable respiratory diseases is still largely an unsolved problem. The gradual exposure of groups rather than sudden exposure of whole camps does not appear practical in the sudden expansion program. Proper spacing in barracks and hospitals and the placing of beds with alternate heads reversed in case the necessary distance for bacteria to travel and materially alter the incidence of infection. The most valuable and difficult task is to decrease the carrier rate. Although previous sprays have not seemed effective a new amacidin spray compound appears promising. The early liberal use of sulfonamide drugs may prove an abortive power, at least in streptococcal spread. Wholesale inoculation with the specific pneumococcal carbohydrate may be effective if such an epidemic is being caused by one type. Probably the most important group to attack is the medical personnel, who are apt to be careless. Vaccinations against respiratory infections should be advocated or it is not possible, special masking and careful hygiene and precautions. The importance of dust is ever increasing. A fine oil spray may prevent easy spread and various germicides sprayed around during bedmaking have met with indifferent success. The use of ultraviolet light as a barrier between beds shows promise for airborne infection only. Eating utensils are a prime source of cross-infection unless properly cleaned, and such clean glass includes running hot water when possible.

The definitive treatment of this group of infections is actually the early and adequate use of the sulfonamide compounds and other drugs. For the intelligent and successful therapy of any infection, the responsible bacterium must be specifically identified. Whereas the pneumococcal pneumonias require only three or four days of intensive therapy, a streptococcal pneumonia with fluid may require one or two weeks or longer. In general, sulfadiazine is the most effective drug, largely because of its water bacteriostatic effect, but also because of its considerably lesser toxicity, which permits more intensive and prolonged therapy.

The consequence of cross-infections even in supposedly clean hospital wards was demonstrated by the development of pneumonias from a different type of pneumococcus in patients convalescing from an original one. In her places, as high as 25 to 35 per cent of patients in clean wards developed positive streptococcal cultures

in their throats, especially during the second and third weeks of convalescence.

BOSTON ORTHOPEDIC CLUB

The annual spring clinic and meeting of the Boston Orthopedic Club was held on May 13, with Dr. O. J. Hermann presiding. The afternoon clinic on various aspects of surgery of the hand was held at the Boston City Hospital.

The first paper, delivered by Dr. J. Edward Flynn, of the Boston City Hospital, discussed Dissections of the Fascial Spaces of the Hand. It was concluded from careful examination of over a hundred dissected hands post mortem that there are always clearly defined mid palmar and thenar spaces. In no case was there absence of the dividing septum. In discussing this paper Dr. Sterling Bunnell, of San Francisco the guest of honor, pointed out that this accurate investigation completely settles any previous conflicts in the anatomy of the fascial spaces. In Dupuytren's contractures, this septum demonstrated by Dr. Flynn is greatly accentuated.

The second presentation, by Dr. Edward Hamlin, Jr., of the Massachusetts General Hospital was entitled The Interruption of the Hand. His conclusions were based on end results from a group of cases at that hospital, in which the outcome was considered good if the patient was able to resume his usual occupation or carry on every day life satisfactorily. In 147 cases, involving the repair of all nerves about 80 per cent were in this category. This is somewhat better than most series, and the best results were obtained in repair of the ulnar nerve, also contrary to the general rule. Both results may be explained on the paucity of injured radial nerves in the group. Furthermore the relative unimportance of the intrinsic muscles of the hand helps to explain the good ulnar results. In general it was found that motor function eventually returned if there was sensory regeneration. One consistently poor result was in the adductor of the fifth finger, probably because of carelessness in splinting.

In repair of an ulnar nerve, sensory function is the primary consideration. Six of these 55 cases became septic without ill effects. Age apparently was not a factor. The time when repair was carried out was in consequential within broad limits. Of 9 cases in which repair was carried out in less than six hours, 8 were successful, whereas 11 of 17 cases repaired after one month were also successful. Four of the latter were done after more than two years, and 1 after more than four years. The average rate of regeneration was 12 mm daily, with extremes of 0.5 and 35 mm. In the unscathed nerves studied regeneration began at eleven weeks and was complete in thirty-six weeks.

In median nerve injuries repair was successful in 82 per cent of cases. That function of the opponens pollicis muscle is not always an infallible test of function when a laceration occurs at the wrist is borne out by the fact that this was normal in 6 such cases. This probably indicates that the muscle is innervated separately or by a twig given off above the wrist. The rate of regeneration was the same as that of the ulnar nerve, and, again, age played no part. However, results became poorer as the time interval between injury and repair increased.

The few cases of radial nerve injury afforded good results in 78 per cent. Results in the recent period, however, were much better than formerly.

In nerve injuries associated with fractures, surgery was seldom required. Good results were obtained in 96 per

cent of cases, and the failures were due to gross inefficiency. It was instructive to learn that such injury followed rather than preceded open reduction of a fracture in some cases. This suggests that although identification of a nerve at operation is an admirable procedure, unnecessary retraction or manipulation merely leads to trouble.

Heretofore, there have been no satisfactory tests of prognosis in nerve injury, and this is a vital phase of the problem. Electrical excitability still affords the best means of evaluating this status of a nerve, and a new use of the galvanic, in contrast to the faradic, current (devised by Dr. Arthur L. Watkins) promises improved predictions regarding the need of operative repair.

Nothing new in nerve-repair technic has been added. It is believed that twisting is of minor importance unless of marked degree. In old cases, the neuroma must be resected and the nerve freed up as much as necessary to prevent tension during regeneration. Splinting is indispensable for the prevention of tension and of the loss of tone in the denervated muscles.

In his discussion of this paper, Dr. Bunnell stated that he had found sepsis of more consequence than here intimated. Furthermore, he considers lack of rotation critical, especially near the field of distribution of a nerve, where the bundles begin to have a definite place. Absence of opponens paralysis in median-nerve laceration is explained by a shift of innervation.

The next paper, by Dr. Henry C. Marble, of the Massachusetts General Hospital, entitled "Infections of the Hand," was devoted to some commonly overlooked problems in this vast field.

The staphylococcal carbuncles and different types of abscesses are usually easily recognized. The streptococcal infections are known to be a wildly spreading process, often heightened dangerously in hospital personnel by human passage. The septic human-bite wound is now being better understood but is still usually seen too late because of the alcoholic euphoria of so many of these patients.

Vaccination has not infrequently been mistaken for chancre or some serious ulcer. Gonococcal tenosynovitis closely simulates that caused by the streptococcus, there being no trauma. This is common in genitoinfectious-disease clinics but is rarely recognized in a hand clinic. About half the cases of nontraumatic tenosynovitis fall in this category when proper studies are done. If there is any suspicion or when there is a tenosynovitis of questionable etiology, a proper bacteriologic setup should be available in the operating room. If this diagnosis is confirmed, any incision should be closed without drainage.

The classic tuberculous joint involvement, with grating crepitation and fluctuation above and below the carpal ligament, is a relatively late stage. At any stage, the problem is essentially a medical one. Dr. Marble now advocates merely splinting and bed rest, the former choice of treatment, surgery, being retained for later use, if necessary.

Fungus infections are becoming increasingly common, and are particularly significant when secondary infection, with its concomitant cellulitis and other sequelae, occurs. This may prove an important field for the use of the relatively new, gramacidin treatment.

An unusual but difficult and interesting injury to treat is the "grease-gun hand," in which grease is pushed into the tissues under tremendous force. These injuries are probably best widely débrided if seen early, but unfortunately they are not often painful or otherwise troublesome for some days or at least hours.

In discussion, Dr. Bunnell stated that he still employs surgery for the eradication of tuberculosis, using wide and careful dissection. The chief advantage is one of speed in convalescence, but even this form may require months of postoperative immobilization. For tenosynovitis, he now employs a "trapdoor" incision over the site of tenderness, in addition to one in the cul-de-sac in the palm. However, it may be possible in the future, with the aid of chemotherapy, merely to carry out the latter incision.

In the next paper, Dr. Champ Lyons, of the Massachusetts General Hospital, discussed "Chemotherapy of Hand Infections." The efficacy of any such treatment is proportional to the accuracy of the bacteriologic diagnosis and the intelligence employed in selecting the kind and amount of drug. Cultures should be incubated at proper temperatures: for example, finger-tip bacteria may grow only under their natural conditions of room temperature. Probably the most valuable single aid is a proper anaerobic medium, of which there are now several simple and efficient ones. Of the streptococci, Groups A, B, C and G all respond to the sulfonamide drugs. Group A, which is the commonest human pathogen, responds to the usual dosage in a short time, but the others should be exposed to higher levels for longer periods. Group D, of which the enterococci are important members, is nonresponsive and is best attacked by zinc peroxide. The staphylococcus, in general, is resistant unless all dead tissue is removed and the drugs are used locally. Human-bite infections, caused by fusobacteria and diphtheroids, are locally necrotic lesions that are treated best by wide débridement. If this is well done, the role of chemotherapy becomes minor. But sulfadiazine in small amounts over long periods has proved efficacious and is even better locally than zinc peroxide. Anthrax lesions respond well to sulfadiazine, but the malignant form should have supplementary specific antibacterial serum therapy. Actinomycosis has now been demonstrated to respond to sulfonamide therapy if this is continued for six to twelve months. Close follow-up examinations are advisable.

In employing local chemotherapy, one should understand that the mechanism of action is not the same as when the drugs are systemically administered. Several factors are involved. The solubility of sulfonamide drugs in serum varies greatly, sulfanilamide being about ten times as soluble as the others and on that account the drug of choice. But the persistence of drug as a foreign body and its cytotoxicity demand consideration. Sulfanilamide is most rapidly absorbed, whereas sulfapyridine has a strong foreign-body reaction. Although sulfathiazole is generally more bacteriostatic and of minor foreign-body irritation, it is highly cytotoxic. This is often overlooked when it is mixed with sulfanilamide. Sulfadiazine is midway between the extremes in all respects and is probably best used as an adjuvant to sulfanilamide, in a 25 per cent solution, especially when dressings are to be more than three days apart.

The final paper of the afternoon, by Dr. William E. Browne, of the Carney Hospital, was entitled "Dupuytren's Contracture." It was emphasized that trauma probably plays a definite etiologic role in certain cases. The pathologic changes usually involve the reticulum layer of the skin as well as the fascia, and skin grafts are therefore often necessary. In dissection, the careful excision of all ramifications of the fascia, especially the deep penetrating ones, is essential. Especial care should be taken to avoid injury to the underlying nerves and vessels and to preserve those supplying the digits.

discussing this paper, Dr Bunnell stated that trauma of direct consequence in pathogenesis. Surgery merely reproduce the original condition unless great is exerted. Certain cases may need stage operations, enotomy may help as an initial procedure. Of the benefit in the postoperative care is the immobilization of the proximal joints.

The evening meeting was held at the Boston Medical Society. Dr Sterling Bunnell, of San Francisco, discussing 'Instruction of the Hand,' emphasized the fact that is 50 per cent of hand injuries are industrial and sensation cases, in which good eventual functional results and immediate saving of time are urgent. Intelligent and well-conceived early treatment may prevent much of the later loss of time and function that is common in neglected cases. Two of the most valuable factors in accomplishing the desired results are the covering of the affected area with skin, even if a flap is necessary, and the positioning of the part in the position of function.

Everything except the affected part is kept in motion. Any surgeon engaged in this field should be trained in orthopedics, plastic surgery and neurosurgery. In general, tendons used in transplants should be of the same as those lost, or improper function may well result. Operations in this field, one must guard against the tendency to open areas of potential infection.

On the original examination of the part, exact figures on amount of function should be recorded, as the result of active and passive motions. The cause of limitation of function, whether nerve, vascular, bone or joint, should be accurately determined and recorded. In general, operations should be carried out in proper stages. Repair of nerves and skin, which requires immobilization of the member, should be done before that of tendons, which demands mobilization relatively early. Every procedure should be considered from the standpoint of its worth while for the patient, doctor and insurance company. All operations on the hand should be carried under a tourniquet and in an aseptic fashion. The hand is 'unbridled' by excision of all flexion contractures. The necessary underlying scar tissue. This also greatly involves the nutrition of the member. Internal scars must be removed en bloc, for these contract just as superficial ones do. Scars of secondary repair should be placed to prevent subsequent contractures and the possibility of dysfunction if keloids form. Although the latter ability of healing is certainly racial and familial to a certain extent, there is increasing evidence that chronic irritation of an early scar probably plays a part.

The appropriate selection of the type of skin graft to be employed and its proper use are very important. On the whole, Reverdin grafts are practically never used, for recipient scar is never strong and may break down on continual usage. Thin Thiersch grafts have many of the vital skin structures missing and very often contract later. But those taken with the Padgett dermatome, thickness of 20/1000 of an inch are about the proper thickness for they develop subcutaneous fat and slide in necessary. It is preferable to employ full thickness skin where there is a possibility of sepsis. The tube type graft is more aseptic than the buried graft and is therefore more frequently used. In placing the skin, one should continually guard against stretching until the graft is white, for in such circumstances the graft will be lost soon afterward. Probably as essential as any single procedure in skin grafting is the guarding against hema-

toma by adequate hemostasis, proper drainage, constant and even pressure, and immobilization.

Nerves account for about 50 per cent of the function of the hand, and their early repair is therefore imperative. All severed nerves as far as the distal crease of the hand should be repaired. No axones are lost, and repair will result in regeneration if nutrition is good. Regeneration of nerves severed above the wrist requires approximately thirteen months, whereas that from wrist to finger tip consumes about seven months. This is about a finger segment a month. Regeneration of sensory nerves occurs irrespective of the time of repair up to about five years, whereas that of motor nerves is more problematical. However, there is nothing to be lost by trying a repair in all cases. In motor nerves, fibrous regeneration starts immediately, but there is little chance of success once response to electrical stimulation is lost. Age is of little significance in nerve regeneration, but nutrition of the part is of the utmost necessity. Nerves should never be immobilized on tension, for this will result in ischemia, with temporary or permanent paresis. In tendon lengthening, the joints are flexed successively and then later extended, starting with the proximal one. Nerve grafts have been successful in selected cases. This procedure is more effective in the smaller, better vascularized nerves, and the sural nerve has proved convenient and of the proper size for the donor site. One should always be careful not to allow axones outside the neurolemma lest subsequent neuromas occur.

Tendons are probably next in consequence to nerves in the hand. Since they do not function in a scar bed, even though they are intact, the scar is removed, and a graft is inserted. One may accomplish this by placing a fascial strip with its slick side toward the tendon, or by the use of the specialized fatty tissue known as 'paratendon'. The best sources of this are over the triceps tendon or under the deep fascia of the thigh. If the area is too cicatricial, an entire tendon assembly in the form of tendon and paratendon from the palmaris longus or dorsum of the foot may be transplanted. The healing of tendon occurs in the following stages: at the end of two weeks, there is connective tissue union, at the end of three weeks, tendon fibers are growing but are not strong, and at the end of four weeks, the tendon fibers are strong. Immobilization does not add to the strength early but looks better, and is therefore usually carried out. But mobilization definitely adds to the strength later. Therefore, the best procedure is to immobilize for about fifteen days to bring about junction without undue reaction and adhesions. Then, the hand is mobilized for strength.

Tendon grafts account for about one third of all operations on tendons. They are usually carried out because of retraction, resection at the time of the original operation, poor tissue or the position of the injury (pulley). The small tendons encountered in the hand require no particular precautions, but large ones need fascia on both sides for nourishment. The palmaris longus tendon is present in 80 per cent of people. The extensor tendons of the toes may be employed, but the brevis should be left for function.

Moving pictures were presented showing the method of suturing tendons at a distance—a method whereby the proximal end is kept from retracting and a few fine silk sutures are all that is required to maintain approximation of the cut ends. Pull-out sutures, which allow strong suture material to be used and later removed after the tendon is firmly healed, are employed.

In conclusion, it was pointed out that the capsulectomy form of arthroplasty is good only for proximal joint fixation, for, in distal joints, instability results. This was in answer to a question concerning the treatment of fixation of disuse. For best stabilization of the wrist joint, removal of the proximal carpal row was suggested.

BOOK REVIEWS

Nephritis. By Leopold Lichtwitz, M.D. 8°, cloth, 328 pp., with 62 illustrations. New York: Grune and Stratton, 1942. \$5.50.

Every physician interested in nephritis may well read this book with interest and profit. No other volume in English affords the kind and amount of information that it contains. It is necessary to point out however, that this is due to the fact that it expresses a highly individualistic and personal point of view—that of Lichtwitz on the kidney. It embodies no comprehensive review of present-day American viewpoints. Furthermore, its point of view, however valid it may be, is one that was reached some years ago. Most of the investigative data on which it is based were gathered before 1925. Of the four hundred and fifty bibliographic references, fewer than thirty concern work done since 1935.

The mere fact that the anatomic studies of such men as Jean Oliver and the clinical and physiologic work of investigators like Goldblatt and his followers, Page, Smith and his collaborators and dozens of others are all but ignored does not detract from the worth of the volume if it is accepted for what it is; the omissions are deliberate. One may be permitted to doubt, however, whether the patient with nephritis will live longer or more comfortably if handled according to Lichtwitz than if treated as he would be treated in any modern American clinic, or even that the state of his kidneys will be better understood. On the other hand, it is refreshing to read a book that totally dispenses with the current pseudomathematical formulas and carefully abstruse jargon of the renal physiologists.

The Principles of Neurological Surgery. By Loyal Davis, M.D., Ph.D., D.Sc. (Hon.). Second edition, thoroughly revised. 8°, cloth, 503 pp., with 154 illustrations. Philadelphia: Lea and Febiger, 1942. \$7.00.

The aim of this book is to give to the average physician and student an insight into what may be accomplished by neurologic surgery as a means of treating nervous diseases. The special branch of surgery dealing with the nervous system is of such recent development that this is one of the first textbooks to deal with the subject as a whole. The author has condensed into a book of moderate size his own experience and the monographic literature on the subject. The result is a sound book, sufficiently detailed for practical purposes and broadly based enough to be of value to all neurosurgeons. The volume reflects, moreover, the rapid strides in neurologic surgery since Horsley removed a cord tumor and Keen a brain tumor, fifty years ago.

The first chapter on diagnosis is the weakest part of the book and might well be omitted from future editions. Subsequent chapters on craniocerebral injuries, tumors, and spinal-cord and peripheral-nerve injuries are sound. The surgery of the autonomic nervous system, epileptiform seizures and essential hypertension are also considered, but with less sureness. The illustrations are adequate. If, as the author, hopes, this book will give the practitioner a better insight into these complicated problems and allow

the patient with operable lesions to reach the hands of the surgeon more quickly, the volume will justify its publication.

A Manual of Allergy for General Practitioners. By Melvin B. Cohen, M.D. 12°, cloth, 156 pp. New York: Paul & Hoeber, Incorporated, 1941. \$2.00.

The boundaries of the field of allergy are still so amorphous that it is extremely easy for the writer of a book on the subject to go astray. We are all familiar with the type of book whose author has been carried away by the esoteric and melodramatic aspects of his cases. The skillful detective work evokes the admiration of the reader but also leaves a residue of doubt and disbelief. The everyday, common-sense practitioner is suspicious of thaumaturgy, since it is not given to most of us to work very many miracles in an ordinary lifetime.

Other books on allergy have lost themselves in the morass of immunology, a subject in which the general practitioner is rarely certain of his depth.

Dr. Cohen has skillfully avoided these mistakes. He has packed an extraordinary amount of useful information into a small space. His style is clear, his definitions satisfying, and his common sense everywhere apparent. Occasionally, in some aspects of the subject,—especially on the importance of bone scorings, taken as an index of active allergy,—there is still some difference of opinion. On the other hand, a small manual is not an arena for controversial subjects, and a rare statement more dogmatic than the circumstances warrant may not be out of place.

For the student or general practitioner who has not yet invested in a textbook of allergy, this manual is an excellent introduction to the subject. For those who wish a working knowledge of allergy, it will more than suffice.

Perineopelvic Anatomy from the Proctologist's Viewpoint. By R. V. Gorsch, M.D. 8°, cloth, 298 pp., with 157 illustrations. New York: The Tilghman Company, 1941. \$8.00.

This is not a textbook of surgical technic but an authoritative monograph of the applied anatomy of the perineum and pelvis from the proctologist's viewpoint. Dr. Lynch, in his foreword, identifies the author as one who is advanced in knowledge of the pelvic outlet.

The text is divided into nine chapters, dealing respectively with the pelvis and pelvic floor, the anal canal, the anorectal musculature, the levatores ani, the rectum and sigmoid, the perineopelvic spaces, the pelvic fascia, the pelvic lymphatics and the nerve supply to the colon, rectum and anal canal. There is a bibliography of selected references at the close of each chapter. The work is based on the author's experience in the practice and teaching of proctology and on a series of excellent personal dissections represented, with some additions from other sources, by many admirable illustrations, some of which are full-page plates, two in colors.

One is glad to note that Dr. Gorsch retains the term "triangular ligament" instead of the misleading modern term "urogenital diaphragm." The occasional errors, which creep into any text, no matter how carefully prepared, will undoubtedly be corrected in a second edition. From the anatomist's standpoint, the work is virtually perfect, and the author is to be congratulated on its successful performance. It will be of lasting value to proctologists and anatomists alike.

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FIVE-YEAR STUDY OF CESAREAN SECTIONS IN MASSACHUSETTS*

ROBERT L. DeNORMANDIE, M.D.

BOSTON

THE completion of the five-year study of cesarean sections in Massachusetts (1937-1941), sponsored by the Massachusetts Department of Public Health and the Section of Obstetrics and Gynecology of the Massachusetts Medical Society, was one to summarize the findings and draw

Over the five-year period, 11,030 cesarean sections and 87 hysterotomies were performed, a total of 11,117 abdominal deliveries. One abdominal pregnancy is not included in this report.

Table 1 shows that 45 per cent of the cesarean sections were emergency and 54 per cent elective

TABLE 1 Summary of Cesarean Sections (1937-1941).

DATA	1937	1938	1939	1940	1941	TOTAL	PERCENTAGE
Total births	61948	64112	64340	68261	73030	333731	
Births in hospitals	48446	50868	52697	56935	63266	272752	
Percentages of births in hospitals	78.5	79.4	81.9	83.4	86.6	81.7	
Cesarean sections	492	2216	1984	2312	2436	11030	
Emergency	872	995	921	1051	1126	4965	45.0
Elective	1178	1196	1059	1247	1309	5989	54.3
Not reported	32	25	4	14	1	76	0.7
Type of operation							
Low	1112	1206	1003	1235	1336	5892	53.4
Classical	80	934	898	992	1009	4033	42.6
Extraperitoneal	20	14	34	26	44	138	1.2
Porro	21	25	26	34	41	147	1.3
Not reported	59	37	23	25	6	150	1.4
In labor	681	744	616	757	806	3604	32.6
Not in labor	1333	1433	1302	1491	1601	7160	64.9
Not reported	68	39	66	64	29	266	2.3
Membranes ruptured	296	331	313	363	387	1695	15.3
Membranes unruptured	1697	1807	1600	1884	2014	9002	81.6
Not reported	89	78	71	60	35	333	3.0
Hysterotomies	24	16	12	21	14	87	
Percentages of abdominal deliveries	3.2	3.4	3.1	3.4	3.3	3.3	

conclusions that might appear arbitrary if based on the statistics of any single year.

The statistics were compiled from replies to sample questionnaires sent to all licensed maternity hospitals, and yearly reports¹⁻⁵ have already been published.

The total number of births reported in Massachusetts during the five years was 333,731, of which 272,752 occurred in hospitals. The percentage of abdominal deliveries was 3.3. It is interesting to note the increase in the number of births occurring in hospitals each year.

operations, with the type not reported in less than 1 per cent. There were more low than classical type operations, but the ratio is not significant. The extraperitoneal and Porro operations account for about 1 per cent each. Sixty-five per cent of the patients were operated on before labor began, but 82 per cent were operated on with membranes unruptured.

The percentage of sections to the total number of deliveries has varied from 3.1 to 3.4 during the entire five years.

Table 2 gives the indications for the 87 hysterotomies. The large majority of these indications seem to be sound. A grave mistake occurred in 2 cases, in which the diagnosis was wrong and a

hysterotomy was done unnecessarily. It is doubtful if the indications "severe bleeding" and "placenta previa at three and a half months" were justifiable.

In Table 3 are recorded the types of anesthesia. Nitrous oxide, oxygen and ether is the type most

ing a normal delivery, but when a study of the questionnaires reveals that in many of the elective sections the babies were very small and obviously premature, it is evident that the time of operation was badly chosen.

I shall speak later of the questionable judgment

TABLE 2. Indications for Hysterotomy.

INDICATION	1937	1938	1939	1940	1941	TOTAL
Cardiac disease	8	7	5	5	6	31
Hypertension or nephritis	4	2	3	9	7	25
Toxemia	2	0	1	0	0	3
Nephrolithiasis	1	0	0	0	0	1
Hydatid mole	2	1	0	0	0	3
Mental disease	1	1	2	2	0	6
Tuberculosis	1	1	0	2	0	4
Neurologic disease	0	2	1	1	0	4
Placenta previa (3½ months)	1	0	0	0	0	1
Severe bleeding	0	0	0	0	1	1
Acute polyhydramnios	1	0	0	0	0	1
Erythroblastosis in previous pregnancy	0	1	0	0	0	1
Fibroid uterus	0	1	0	0	0	1
Separated symphysis	0	0	0	2	0	2
Error in diagnosis	2	0	0	0	0	2
Not reported	1	0	0	0	0	1
Totals	24	16	12	21	14	87

commonly used. The only other point to be noted is the marked increase in the use of spinal anesthesia. The widespread use of local anesthesia in cesarean sections has never been received with favor in this community. It is unfortunate that

shown in performing sections on known monstrosities, which could well have been delivered by vagina.

Table 4 records the indications for sections for the five-year period. Previous section, of course

TABLE 3. Types of Anesthesia.

ANESTHETIC	1937	1938	1939	1940	1941	TOTAL
Nitrous oxide, oxygen and ether	1343	1533	1255	1355	1244	6730
Ether	348	260	194	261	272	1335
Cyclopropane	103	159	136	144	166	708
Spinal	85	106	185	396	641	1413
Nitrous oxide and oxygen	81	19	18	5	8	131
Avertin and nitrous oxide, oxygen and ether	50	29	29	27	15	150
Local	37	34	22	32	62	187
Other	21	50	135	70	15	291
Not reported	14	26	10	22	13	85
Totals	2082	2216	1984	2312	2436	11030

11 deaths have to be recorded as due to the anesthetic.

In each year's study, operations resulting in the deaths of babies have been analyzed under emergency and elective sections. In the emergency classification, 741 babies were lost, and in the elective group 245—a total of 986. To analyze all the indications for the five years would be a lengthy process, but it must be noted that almost 50 per cent of infants were lost because of placenta previa or separated placenta. One questions the advisability of many of these operations, for they were done at six or seven months' gestation and could undoubtedly have been managed satisfactorily by vagina.

It must also be noted that many babies died or were stillborn following elective sections. It is fair to assume that some would have died follow-

tops the list. In this group, many babies were lost from prematurity because the operation was done by election too early in the gestation or because labor had begun prematurely. These possibilities must be kept in mind in all repeat sections. The next largest group comprises patients with a contracted pelvis or disproportion. In many cases, this indication was probably justified, for it was frequently noted that the baby weighed under six pounds, and often the patient did not even go into labor.

About the next two indications, placenta previa and separated placenta, one can only say that there was bleeding. Many of these babies were lost. The number of patients operated on at six and a half to seven months raises the question whether all these sections were necessary. The frequency of fetal malformations in cases

placenta previa makes an x-ray examination advisable before operation for this indication. The majority of operations in the next group—because of an increasing, severe toxemia. Many of these pregnancies were allowed to continue too long, with the result that some of the

necessity for operation. If the cervix has been amputated, it should be known before labor begins, and an elective section performed.

Under "associated medical condition," the largest group was for cardiac conditions. The necessity or even the advisability of operating in many

TABLE 4. *Indications for Cesarean Section.*

INDICATION	1937	1938	1939	1940	1941	TOTAL
Previous section	576	635	608	726	722	3267
Contracted pelvis or disproportion	539	477	336	350	491	2193
Placenta previa	183	175	215	211	237	1021
Separated placenta	77	104	86	109	106	482
Toxemia	123	125	78	107	114	547
Eclampsia	10	9	11	15	8	53
Malposition of baby	68	110	79	113	109	479
Dystocia	94	202	220	279	246	1041
Previous surgical operation	45	43	36	56	50	230
Associated medical condition	59	61	51	51	46	268
Previous obstetric disaster	64	47	52	73	76	312
Elderly primipara	48	70	58	57	58	291
Obstructing tumor	15	18	24	21	44	122
Fetal distress	5	7	6	7	11	36
Prolapsed cord	9	3	4	4	7	27
Following operative attempt	1	7	7	8	10	35
By request or for sterilization	27	17	10	9	10	73
Ruptured uterus						
Spontaneous	1	1	2	2	2	8
Previous section	1	7	6	2	4	20
Abnormality of genitourinary tract	3	4	2	3	7	19
Twins	2	0	0	3	5	10
Postmaturity	8	4	3	8	8	31
Malformation of fetus	1	2	0	1	1	5
Varicosities of vulva	5	0	0	3	0	8
Unengaged or floating head	0	1	0	0	1	2
Congenital dislocation of femur	0	6	0	0	1	7
Fractured pelvis	0	0	1	0	1	2
Error in diagnosis	0	0	1	0	1	2
Surgical emergency	0	0	1	0	1	2
Early rupture of membranes	0	0	0	2	0	2
Young primipara	0	0	0	1	0	1
Multiparity	2	0	0	0	0	2
Prolapse of uterus	2	0	0	0	1	3
Premature labor	3	0	0	0	0	3
Feeble-mindedness	1	0	0	0	0	1
Social and economic reasons	0	3	0	0	0	3
Abdominal hernia	0	1	0	0	0	1
Obesity	0	1	0	0	0	1
Desire for living baby	0	1	0	0	0	1
Frequent miscarriages	0	1	0	0	0	1
Bizarre	55	25	32	19	19	150
Not reported	47	48	52	63	39	249
Totals	2082	2216	1984	2312	2436	11037

mothers died. One cannot help believing that if we were more careful prenatal care, fewer patients would be operated on for this indication.

It is surprising that eclampsia should have been an indication in 53 cases. Eleven mothers (21 per cent) and 9 babies were lost, a very high mortality.

An increasing number of sections occurred for each presentation. Many of the patients were multiparas, and the babies were of moderate size. It is obvious that when any malposition appeared, there was little attempt to manage it by vagina.

Under "dystocia," I have included the so-called "stagnant labor" cases. In the latter part of the century, there were many more attempts to give the patient a test of labor. Some cases of so-called "dystocia" had no labor whatsoever.

The majority of sections because of previous surgical operations were for repairs of the perineum and cervix. Again, there is no way of judging the

cardiac cases is open to question, for it is known that such patients often have short, easy labors. With careful management, they may be better delivered by vagina. Careful consideration of all factors is necessary before the decision to operate on a cardiac case is made.

Kidney complications, central-nervous-system disease and tuberculosis were some of the other medical indications. Because one clinic believes that many diabetic patients should be delivered by section, the frequency of this indication has increased.

If operation seems indicated with a history of previous obstetric disaster or difficult operative delivery, it should be elective or should follow a short test of labor under careful supervision. Labor for eighteen to twenty-four hours without progress, followed by an emergency operation, should never occur with this indication.

It is impossible to judge whether all the elderly primiparas required sections. If the indication is real, however, it should be an elective, not an emergency, section.

Obstructing tumors should be discovered by careful prenatal examination, and operation for

For the next indication, "malformation of fetus," 19 sections were done with a known malformation present. Accompanying this indication, there was no statement that the patient had a contracted pelvis. Unless there is some other indication, section on a known malformation seems to be

TABLE 5. *Summary of Maternal Deaths in Cesarean Sections.*

DATA	1937	1938	1939	1940	1941	TOTAL	PERCENTAGE
Total maternal deaths	66	60	54	41	52	273	2.46
Emergency	51	39	45	33	36	204	74.7
Elective	15	21	9	8	16	69	25.2
Type of operation							
Low	29	26	24	15	16	110	40.0
Classical	29	24	26	20	30	129	47.4
Extrapertoneal	4	2	2	2	3	11	4.0
Porro	2	3	2	1	3	14	5.1
Not reported	4	5	0	0	0	9	3.0
In labor	31	25	29	22	20	127	46.5
Not in labor	32	30	25	19	32	138	50.5
Not reported	3	5	0	0	0	8	2.9
Membranes ruptured	13	18	15	17	13	76	27.7
Membranes unruptured	47	37	39	24	39	186	68.0
Not reported	6	5	0	0	0	11	4.0
Babies							
Living	43	43	42	36	40	204	73.8
Dead	23	17	12	8	12	72	26.1

this indication should also be elective, not emergency, as often happened.

Only 3 babies were lost following section for fetal distress, and 5 for prolapsed cord. One wonders whether the fetal distress was real. Undoubtedly, cesarean section for prolapsed cord will save a certain number of babies, but the infant mortality rate for this indication was 18 per cent.

A section following operative attempts at delivery is a serious procedure. Although a certain number of mothers and babies may be saved, the mortality rate is high. In this group of 35 patients, 10 mothers and 11 babies died.

I cannot consider the next indication justifiable. Yet 73 operations were done at the request of the patient or for sterilization.

Comment on the indication "ruptured uterus" is unnecessary, for the patient with this condition must, of course, be operated on as quickly as possible.

Under "abnormality of genitourinary tract," a surprising number were bicornate uteri.

"Twins" was the recorded indication in but 10 cases. Many other cases of twins occurred, but the operation was for some other indication. In a few of these, "disproportion" was given as the indication, no x-ray film was taken, and twins were delivered. There were 2 cases of triplets.

The indication, "postmaturity," is specious, especially when, as happened several times in this series, a baby weighing 7 pounds or less was delivered.

entirely unwarranted. The surgeon should ask himself whether he would like his wife to be operated on for a known malformation of the fetus incompatible with life; I think the answer is clear. No religious dogma demands that a section be done under these circumstances. In 1 case in which a section was done, the hydrocephalic head was so large that it had to be punctured before it could be removed from the uterine incision.

Under "unengaged or floating head," 8 cases were operated on without any labor, again an unjustifiable procedure.

If congenital dislocation of the femur has so narrowed the pelvis that a baby cannot be delivered through it, that indication is of course real. The same thing is true of fractured pelvis.

It is unnecessary to go through each of the other indications. It is seen at once that some are questionable. Under the heading, "bizarre," 150 cases have been grouped. A few will serve as examples: "pregnancy at term," "Braxton-Hicks contractions," "highly nervous state of the mother," "pain in right hip" and "threatened placenta previa." I might go on with many other equally bizarre indications.

Table 5 presents a summary of the maternal deaths. In making this study concurrently with the five-year study of maternal mortality in Massachusetts, it has been possible to obtain data concerning the deaths from cesarean section from the

ernal-mortality investigations of the same cases, which were made by physicians in personal interviews. This has given a much more accurate picture of the cesarean deaths than the questionnaires would have revealed. As a result, in many cases, the causes of death given on the questionnaires have been found inaccurate, and the causes of death from the maternal-mortality schedules have been accepted.

Over the five-year period, there were 273 deaths. Of these, 74.7 per cent followed emergency operations, and 25.2 per cent followed elective sections. Over patients were lost following low than classical sections, but I am inclined to think that the reason the classical type was performed more frequently is that it can be done more quickly in an emergency.

Eleven patients, or 4 per cent, died following extraperitoneal operations. Some were undoubtedly selected cases. Others were under observation by competent physicians the entire time, and yet they were allowed to remain in labor so long that the physicians were forced to do extraperitoneal operations resulting in death. In this operation, there is danger of opening the bladder or cutting the ureter, as was done in this group.

Fifty per cent of the deaths followed a Porro operation. The majority of these were done for fibroids or an atonic uterus.

Table 6 shows the causes of the maternal deaths. A total of 273 deaths gives a mortality rate of

TABLE 6. Causes of Death in Cesarean Sections.

CAUSE OF DEATH	NO OF CASES	PERCENTAGE OF TOTAL
Sepsis	106	38.8
Hemorrhage	32	11.7
Embolus	23	10.0
Shock	25	9.1
Cardiac	17	6.2
Anesthesia	11	4.0
Eclampsia	10	3.6
Acute respiratory infection	8	2.9
Toxemia	7	2.5
Anaphylaxis	6	2.1
Intestinal obstruction	4	1.4
Acute pulmonary edema	4	1.4
Premature separation of placenta	3	1.0
Miscellaneous (1 each, chronic nephritis, toxic purpura hemorrhagica, thyrotoxicosis, superior mesenteric thrombosis, scarlet fever, acute yellow atrophy, anuria, uremia, surgical emergency, carcinoma, no adequate cause and not reported)	12	4.3
Total	273	

16 per cent, a remarkably good record. I doubt any other state has excelled it. Analysis of the statistics, however, shows some disturbing facts.

One hundred and six patients, or 39 per cent, died from sepsis. Of these, 24, or 23 per cent, were elective sections. It was in these cases that most of the changes were made in the causes of death. The following history is typical. Immediately following operation the patient's temperature and pulse rose. There was distention, vomiting and delirium, and death followed. The questionnaire gave the cause of death as "toxic myocarditis, vasomotor collapse and paralytic ileus." Interview by the investigator in the maternal mortality study brought out the true facts. The desire to cover up the diagnosis of sepsis led to improper certification of the cause of death.

Hemorrhage accounted for 32 deaths, or 11 per cent. The majority of these followed section for either placenta previa or separated placenta. Often, when a section has been done for separated placenta and bleeding continues, a quick decision must be made whether or not to remove the uterus to save the patient. In several cases, the uterus failed to react, and yet the surgeon did not remove it. Several patients died from postpartum hemorrhage two or three hours after operation, which suggests a lack of careful nursing supervision.

There were 28 deaths, or 10 per cent, from embolus. Some of these patients had a definitely septic chart, and although the death was undoubtedly due to embolus, it might well be classed in the septic group.

Shock was given as the cause of death in 25 cases, or 9 per cent. It was frequently difficult to determine whether death should be assigned to shock or to hemorrhage.

In many of these fatal cases, no donors were provided for transfusion. In one case, the operation was done by a general surgeon; the patient bled profusely during the operation and continued to bleed afterward; yet the surgeon left the hospital as soon as possible after the operation, and made no attempt to stop the bleeding. The local physician was unable to cope with the situation, and the patient died from postpartum hemorrhage. On the whole, however, the use of transfusion has been gratifying and has undoubtedly saved many lives.

The death of 11 patients, or 4 per cent, from anesthesia is a serious criticism. Careful anesthesia must be provided in all cases. I have already spoken of the cases of eclampsia and toxemia. Some of the latter were elective sections, and the patients should not have been lost.

The deaths from acute respiratory infections were accidents and could have been avoided only by the most meticulous care.

Of the anaphylactic deaths, 1 resulted from what is called "pituitary shock." The other 5 were classified as due to improper matching of blood. That statement must now be revised in the light of the recent work on the Rh antibody.

It is fair to state that these reactions may have been due to this newly discovered factor.

That 4 deaths should have been caused by intestinal obstruction was undoubtedly due to lack of keen observation on the surgeon's part.

In the cases of acute pulmonary edema, it is noted that the patients were operated on after they had been in labor a very long time.

Although only 3 deaths were assigned to premature separation of the placenta, this complication occurred in some cases in which the death was assigned to other causes.

The miscellaneous list of 12 causes of death needs little explanation. The scarlet-fever case was apparently true scarlet fever, and the surgical emergency was one in which there was an aneurysm of the splenic artery, which ruptured. In the death assigned to acute yellow atrophy, the patient had an unusual blood condition and bled from the gums, stomach and other mucous membranes. The uremic case was one in which the patient had had one kidney removed, developed toxemia during pregnancy and gradually failed, with an increasing nonprotein nitrogen. The death assigned to carcinoma was that of a patient whose entire pelvis was involved with cancer, the section being done to save the baby.

* * *

This is the largest series of cesarean sections ever reported from one community, so far as I have determined, and the results are remarkably good. Examining them superficially, one could not criticize them. But on analysis, one must conclude that many unnecessary cesareans were done. Because of this, the number of repeat sections will continue to increase and will always give a certain number of deaths. The same criticism is true regarding the indication "contracted pelvis or disproportion." There is no doubt that many physicians do not carefully study each case. Cesarean section is an easy way out of a

difficulty, but it often has serious consequences for the mother in future pregnancies.

The fact that nearly 40 per cent of the patients died from sepsis is a very serious criticism of the medical profession. It shows conclusively that there was either error in technic or in the choice of a method of delivery. In some cases, when a low or classical section followed a long labor, sulfanilamide was used in the abdomen. Many of these patients eventually recovered, even though the convalescence was stormy. It is conceivable that this will become a routine treatment in emergency cesareans with a possibility of infection, and that the percentage of septic deaths may thereby be greatly reduced.

The maternal mortality rate for these cesarean sections, 2.46 per cent, was low, but when one realizes that in the maternal-mortality study, cesarean section figured in nearly 20 per cent of the deaths, it is evident that such deaths are a potent factor in keeping the State maternal mortality higher than it should be.

In closing, I want to thank the hospitals that co-operated so splendidly in making out their questionnaires. It added a great deal to the work of their record rooms. In nearly all cases, it was well done, and the true facts were reported. Only in a few cases was there lack of co-operation; this occurred chiefly when the physician obviously wished to cover up poor obstetrics.

Under the new law making the Department of Public Health responsible for licensing all hospitals, and with an investigator checking their records and procedures, one can look forward confidently to even better results.

330 Dartmouth Street

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TRAUMA OF THE SKIN DUE TO WARTIME ACTIVITIES*

JOHN G. DOWNING, MD †

BOSTON

IN emergency came, and we were found wanting. It must never happen again! Preparedness must be our watchword, not only for defense but also for offense when the opportunity arises. Physicians must be prepared to relieve and prevent injuries due to wartime activities. No longer may the specialist be content to confine his study to the immediate realm of his specialty—he should be trained for any emergency. While lay persons, because of their attendance at various courses, are only talking of poisonous gases and first aid, many medical men still remain ignorant of some of the essentials of both.

Care of the skin is vital at present. During the Spanish Civil War, cutaneous disease caused undue suffering and disability in civil and military populations, and helped to decide the outcome of the war. The same diseases played a great part in World War I.

Medicine has learned tragic lessons from these experiences, but there are still many pitfalls to be avoided. It has been stated that in war will be one of industry and production. The producers must therefore be kept healthy—at least, occupational diseases, of which dermatoses comprise 60 per cent, must be prevented. President Roosevelt, in a recent newspaper interview, expressed his alarm over this aspect of industry: 9,000,000 man days of work lost; 101,800 persons killed; 350,000 permanently disabled—1 out of every 14 workers, most of them from twenty-one to forty-four years of age, or enough to build several battleships or equip several regiments. The President hoped that everyone would reflect on these figures, so that the situation might be remedied or at least improved, and he must have had medical men particularly in mind.

New plants are being equipped, and old plants are experimenting with substitutes, new chemicals and chemical processes. Speed is essential to fill contracts within specified time limits, but reckless haste results in disaster. Overcrowding in factories and in the housing of workers must be avoided. Although the older and larger plants are properly prepared, others lack adequate preventive methods, such as means of ventilation and exhausts, and many factories have no facilities for the personal hygiene of the workers and no medical supervision. Too few physicians are prop-

erly trained to cope with these problems, and still fewer have sufficient knowledge of industrial poisons. Recent events created a national emergency that subordinated the welfare of the individual to that of the Nation. Nevertheless, it behooves the physician to watch the individual, for each person affected may be a warning of the imminence of an epidemic of disabling dermatitis of physical, chemical or infectious origin, whether in civil, industrial or military life. At present, it may seem strange to assert that, of the three groups, the industrial is the most important. Yet it is reasonable to believe that the loss of one key worker may delay the necessary equipment of many fighters. Hilliard¹ points to the need of a public health program and states that there are the same possibilities of reducing sickness among industrialists who congregate daily as there are in preventing diseases in the general community. At present, the most essential wartime industrial activities are the manufacture of garments, machinery, tools and explosives, aircraft production and shipbuilding.

OCCUPATIONAL DERMATOSES

Recognition of an industrial dermatitis may often prevent similar occurrences in military life. For example, an outbreak of dermatitis in a plant making raincoats was shown to be due to free sulfur. To hasten production, the rubber was semicured, resulting in the release of the free sulfur and causing erythema and intense itching of the skin of many employees. Such coats would have irritated the soldiers wearing them.

In another plant manufacturing rubber goods, it was found that the old rubber cement could not stand the intense heat essential for the rapid turnover, and a new cement was therefore introduced. The cementers encircled a wad of the rubber cement around their right index fingers and applied it to the seams and edges. They suffered a dermatitis consisting of edema, desquamation and fissuring of the fingers, with extension of a sensitization eruption over the hands and arms, with resulting disability and loss of production.

In April, 1940, I investigated the cause of an epidemic of cutaneous diseases among boys and men wearing new fabrics. Each eruption started with marked erythema and edema of the penis and then of the scrotum; later, vesicles and wheals appeared on the loins, and the rash frequently be-

*Presented at the annual meeting of the Massachusetts Medical Society on May 26, 1942.
†Visiting physician for diseases of the skin, Boston City Hospital.

came generalized. It was accompanied by such intense pruritus that one patient became temporarily violently insane, so that it was necessary to commit him to a psychopathic hospital. The

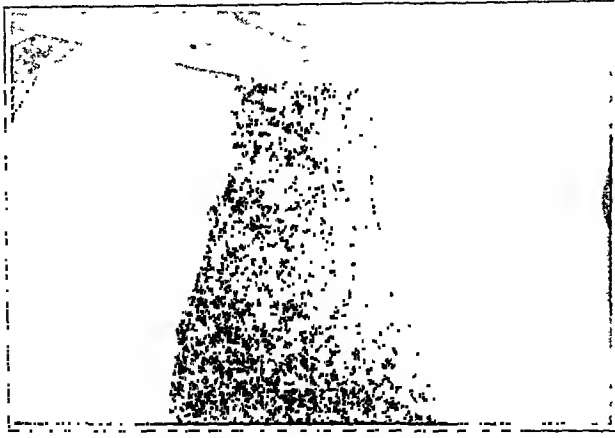


FIGURE 1. Painful Heels due to Cement in Shoes.

The skin appears white and sodden, like boiled meat. A physician suffering from this disturbance was willing to undergo a sympathectomy for relief; change of footwear avoided this.

causative factor was found to be a new synthetic resin finish that had previously affected the employees in textile industries. The same finish had



FIGURE 2. Leather Dermatitis.

An eruption on the distal half of the dorsum of the foot should suggest such a diagnosis, rather than that of a fungus infection.

been applied to cloth intended for the army personnel, but was withdrawn and not issued after this investigation. It would have caused more disability than a horde of Japanese.

In another textile plant, two workers handling indigo cloth for sailors' blouses suffered a dermatitis from a change of the formula. Sensitivi-

ties to these clothes should be kept in mind, for they are already appearing in the coast guard and naval personnel.

Shoe workers are still suffering from hazards incident to their trade, and eruptions are occasionally seen from footwear (Figs. 1 and 2). These patients are usually treated for fungus infections, owing to mistakes in diagnosis.

Among machinists and their helpers, dermatides from cutting oils have become unnecessarily numerous (Fig. 3). The cutaneous manifestations have been of two types: mechanical interference with bodily function, that is, folliculitis; and the reaction of hypersensitivity, that is, eczema. In the first group, the skin becomes dry and scaly,



FIGURE 3. Folliculitis from Cutting Oils.

The skin shows a breaking off of the hairs, papules and pustules.

and the lanugo hairs break off at the point of emergence from the follicles, leaving a black-dot appearance; comedones result from the collection of epithelial debris and dirt; later, acuminate papules, which become secondarily infected and form pustules, furuncles and large abscesses, appear. These heal with scars varying from smooth pigmented atrophy to large keloids. In the second group, the eczematous dermatitis is localized or generalized. Men assembling small parts work with their hands close together and suffer erythematous, dry, fissured eruptions of the hands, because of constant contact with the drying oil. In the assembling of large parts, the oil splashes on their arms and clothing, and the eruption appears on the arms, especially in the antecubital spaces and on the abdomen and the anterior aspects of the thighs. Admixtures such as terpenes, creosols, acids and alkalis are usually the sensitizers. Minute pricks from metal chips produce portals of entry for bacteria, with resulting pyoderma. Cancers are infrequent.

Similar eruptions appear in workers exposed to chlorinated naphthalene, such as men handling

bles containing halowax used for insulation of wires. This is especially true in poorly ventilated places, as in ships under construction. In these exposures, the workers must be watched because of the danger of systemic poisoning. Six electricians working in a submarine developed yellowish, wax-like milia on the sides of the neck, the lobes of the ears and the cheeks, accompanied by comedones, papules, pustules and nodules (Fig. 4).



FIGURE 4. *Acneform Eruption from Halowax.*

The skin shows yellowish, wax-like milia, comedones, papules, pustules, and nodules.

Two had similar lesions on the forearms and thighs. No systemic disturbances were discovered after careful physical examination and laboratory studies.

In the manufacture of explosives, trouble rarely occurs among the older employees, but new workers, who may not be immune and who do not realize the danger in handling the various materials, sometimes neglect to take the proper precautions. Dinitrotoluol and the nitrates, especially ammonium nitrate, are cutaneous irritants, and the workers who mix them develop a dermatitis. Fulminate of mercury is used in the making of detonators and percussion caps. Workers exposed to this compound may show signs of mercurial absorption, and those who perspire freely may suffer an affection of the skin of the neck, behind the ears, of the face and in the antecubital spaces. There is inflammation of the nasal mucous mem-

brane, the skin is discolored, and there may be shallow ulcerations at the tips of the fingers that are relieved by 10 per cent sodium hyposulfite. Tetryl and trinitromethyl nitramine also cause eruptions among new workers. An eczematous dermatitis appears at the edges of the respirators and the volar surfaces of the forearms. Two types of cutaneous eruptions may appear: mechanical interference because of the penetration of the dust into the follicles and the microscopic punctured wounds caused by the sharpness of the crystals; and sensitization dermatitis—that is the chemical may be dissolved in the fluid from the seborehelic areas and produce inflammation of the skin, most marked in those areas.²

Trinitrotoluene causes a marked deep-orange staining of the skin, by which it is readily absorbed. In the summer of 1919, I treated many cases of poisoning contracted in unloading depth bombs, but only a few cases of active dermatitis were observed. One of those affected was seen two years later, when he was operated on for what was thought to be gall-bladder disease but was actually yellow atrophy of the liver. Trinitrotoluene causes a blue hue on the gums similar to the blue line caused by lead poisoning. This disappears after removal from exposure.³ A few hours' exposure on a hot day often results in cyanosis, with marked blueness of the lips. Dinitrophenol causes not only local but also systemic disturbances. Explosives, especially those containing potassium dichromate, also affect the mucous membranes, causing perforation of the nasal septum. Nickel and chrome plating are frequent causes of dermatitis. Substitutes are being used in every plant; for example, benzol is now being employed for toluol and may result in blood dyscrasias and cutaneous hemorrhages. Hydrofluoric acid, mercury and magnesium are widely used and all affect the skin.

In airplane manufacture, the agents responsible are: all the halogens; the fish oil, covering the duraluminum, which is laden with bacteria; volatile substances from the paint shop, thinners, dope, special formulas, fumes, varnishes, solvents, gasoline, dryers, asphalts, dyes and oils; and cutting oils in the machine shops (neutral petroleum with free sulfuric acid). Contact with acids, iron oxide, emery, rottenstone and chrome polishing agents may be injurious.⁴ Chromic acid compounds cause punched-out ulcerations of the skin and nose, as well as eczema. All the above apply as well to the shipbuilding industry.

In military life, the possibilities for cutaneous diseases are similar to those of industrial and civilian life, varying from sensitivity to clothing and baker's eczema from cinnamon powder or the

persulfates to burns from explosives and gases and infections regarded in civil life as trivial and belonging to the unwashed. However, in military encampments, especially on active service, these diseases become of major consequence, owing to close crowding of men and lack of suitable bathing facilities. Pediculosis vestimentorum capitis and pubis, rarely seen in private practice, infested the personnel of entire camps during the last war, causing great discomfort and severe secondary infections, and were carriers of disease. It is difficult to guard against the single soldier who unknowingly introduces this parasite into a camp. Scabies also caused the loss of many man-days, through failure to recognize the disease and through over-treatment. Scabies alone may be only disconcerting and not disabling, but when combined with sepsis it causes real disability. Every persistent or widespread furunculosis should be regarded as having scabies as a background until such a basis is disproved. Ecthyma and severe pyoderma may result from parasitic infestation.

Fungus infections of the skin are already becoming a problem in the various camps. Before the last war, such infections were endemic in various parts of the tropics. Hence, it was brought by seasoned veterans to training camps, and widespread infection occurred. In turn, these men on discharge brought it to their various communities. The original foci appear harmless: an area of maceration between the toes, especially in the fourth interspace, a few deep-seated vesicles on the central arch of the foot, a yellowish hyperkeratosis under the anterior arch, or a thickened toenail plate may be overlooked or passed over by the examining medical officer. One such focus may infect a whole company. This focus, after a long march or days of sleeping with shoes on, may assume alarming proportions, resulting in the so-called "trench feet" of the last war, or a lymphangitis, an encircling erysipeloid eruption of the lower legs, a phlebitis, inguinal adenitis or even a cellulitis, with resulting serious illness. The fissures caused by fungus infections are frequently portals of entry for streptococci and staphylococci. In this war, world wide as it is, medical officers should be cognizant of fungus infections. At least, they should know those endemic to the neighborhood of their camp, a necessity made evident by the recent outbreak of coccidiosis at a camp in California.³

EXPLOSIVES AND GASES

Medical officers and personnel are being trained to cope with the more obvious products of modern warfare, the dangers of explosives and gases. These men are equipped and have adequate protection against gases known to exist, and are therefore

ready for any such onslaught; civilian physicians and populations should likewise be informed, trained and equipped. Bit by bit, we are losing our sense of security derived from distance, but this distance still seems to nourish the hope that it would not be worth while to transport wartime gases so far. Why not? They certainly would be sure and as effectual as incendiary bombs. Such an unfamiliar danger could cause great terror and panic. A hit is not necessary—dropping the gas in the vicinity of a plant is enough to disrupt its production at least temporarily. Its effectiveness was demonstrated in the last war. Why have they not been used in this war? It cannot be because of previous treaties, all of which have been flouted; it cannot be because of fear of retaliation, for no such fear on the part of the aggressor has as yet been apparent; it cannot be because of solicitude for the civilian populations, for the bombing of Rotterdam and Coventry belies any such solicitude. It is probably because the rapidity of action to date would make the most valuable gases, the persistent ones, more dangerous to the user than to the enemy; or perhaps up to date the aggressors have not felt the need of these gases and are holding them in reserve in case of necessity. Perhaps the element of surprise, which seems essential in this conflict, would be lacking, for unless the aggressors have developed a new gas they believe that the civilian and military populations are prepared. The time may come when necessity or opportunity or a new discovery will determine their use. I believe that warfare gases will be used on the civilian populations rather than the military, and it consequently behooves physicians to keep informed of progress in this field.

Although many thousands of gases were investigated up to 1918, only a few were found to be effectual, and almost without exception these contained bromine or chlorine atoms. They are effective because of their irritant or destructive action on the skin and mucous membranes. The five most deadly ones are mustard gas (dichlorethyl sulfide), lewisite (vinylchlorazene), phosgene, chloropicrin and bromobenzyl cyanide. Lewisite was not used in the last war. Most of the gases are liquids that, when dispensed as droplets, persist for a long time. Mustard gas, which was the most widely used and was the most effectual, causing the greatest damage to the skin, penetrates paint, woodwork, porous material, shellac, paper, wax, leather and ordinary clothing. Oilskin clothing and synthetic rubber are penetrated slowly.⁴ It belongs to the vesicant group—that is, those that cause vesiculation or blistering of the skin. They all present a similar clinical picture—erythema in the folds of the skin, most marked about the geni-

neck and axillae, vesicles and bullae appearing idly. The depth of penetration varies. Persons differ in their sensitivities and reactions to these, so that the lesions may range from simple incrustation to necroses, depending also on the concentration and period of exposure.

Mustard gas and lewisite are the most important vesicants. The former causes edema of the lungs, pseudomembranous pharyngitis and destruction of cells and tissue. In civilian populations, chemical warfare is more complicated because of the different ages of the population, and on account of various diseases. Early symptoms may be sneezing only; gradually, the throat becomes irritated. In about twelve hours, there is a discharge of mucus from the nose. At the same time, the early cutaneous lesions appear. The older burns are more frequent and insidious, and appear slowly. They are erythematous plaques resembling sunburn. After a while, the central portion desquamates, leaving a slight weeping surface, without any actual blister formation. The most serious lesions are likely to be severe, and are followed by erythematous patches covered with large bullae containing a serous or seropurulent fluid. They occur on the flexor surfaces, particularly about the scrotum, and are frequently preceded by small pustules surrounding the hairs. The pain is commonly severe. Occasionally, necrosis occurs. Itching replaces the pain and may persist indefinitely, being continued by a traumatic neurosis. I have three veterans under treatment who, since 1918, have had pruritus due to mustard-gas burns. Lewisite acts more quickly on the human skin. The latent period is only fifteen to thirty minutes. Its minimum irritant concentration is below its perceptibility through odor. It is apparently absorbed through the skin, causing systemic poisoning. At first, there is a slight burning sensation. After thirty minutes, erythema of the skin occurs and increases gradually. After three hours, areas from 12 to 15 cm. are affected. After thirteen hours, numerous blisters, cherry size and smaller, appear and gradually coalesce in one large blister,⁷ which later becomes surrounded by an erythematous halo. These areas may slough down to the muscles, and unlike mustard gas, which usually leaves only atrophy, lewisite may result in deep scarring. The pain accompanying these burns is usually severe. I have already seen one patient with a burn from lewisite. He was an instructor who demonstrated the art of sniffing once too often. He showed marked erythema and desquamation of the skin on the face and neck. Death may occur from both uses, but more frequently results from lewisite.

Burns from caustics have been seen particularly from sodium hydroxide, which causes lesions varying from a few vesicles to deep ulcerations (Fig. 5). With the maintenance of military secrets, it



FIGURE 5. Punched-out Lesions from Caustics.

is impossible for the outside physician to know exactly what the exposure is, but careful scrutiny of the skin—especially of the hands for yellow, brown or gray stains, or a bluish appearance of the mucous membranes, or punctate hemorrhages—will lead to the suspicion of systemic poisoning.

PREVENTION

Most occupational dermatoses can be prevented. Hazards must be detected and eliminated. Mechanical devices should replace manual contacts, and when this is impossible, gloves should be worn; when gloves cannot be worn, protective liquids or creams should be tried. Such creams must be selected with care, for they can cause eruptions. Workers exposed to irritants and oils should be taught the value of cleanliness, not only of themselves but also of their benches and machines, and of removing the grime before meals and of applying an emollient at bedtime, and again before starting work. Periodic instruction to foremen is highly recommended; they should be taught the need of careful supervision of their men and women workers, so as to prevent them from discarding gloves and from using dangerous short cuts to speed up piecework, such as dumping articles in bowls of acids or caustics and removing them by hand instead of by tool, as well as using fingers, cloths or sponges in place of brushes.⁸ They should watch for signs of fatigue or carelessness or recklessness, all of which are the chief causes of many injuries. Hazardous processes should be safeguarded whenever possible. No new substances should be introduced until their possible effects on the workers have been thoroughly studied. In

many cases, dangerous chemicals are preferred to less irritating ones because of their lower cost—for example, the use of benzene instead of naphtha; moreover, since many chemicals are not now available, substitutes must be used. No worker should be compelled or permitted to keep his hands wet with any solution for hours at a time, for few skins can stand constant wetting. Such jobs should be alternated during the day with those in which the hands must be kept dry. Young workers, notably those under twenty years of age, should not be employed in hazardous occupations, such as the manufacture of explosives.

In military medicine, the best method of prevention is the instruction of medical officers in the early recognition of dermatoses, careful inspection of newcomers to camp and segregation of those with contagious cutaneous disease. Treatment of these diseases should be by recognized, proved therapy. Experimental work should not be tried at military camps, but at home by those who are unable to enter active service. Perforce, much will be learned, by accident or by mistakes. It is already known not only that the sulfanilamides are neither bactericidal nor fungicidal but also that both organisms will grow in their presence. They must be used with care, especially in persons who have industrial exposure to magnesium or sulfate. I have seen one case of a generalized dermatitis following the ingestion of two tablets of sulfathiazole in a worker who had such an exposure. Whether this was due to a peculiar idiosyncrasy of the patient who had never taken any medication or to this exposure is impossible to state. Their use locally should be limited to fresh preparations or those sterilized.

Physicians must be alert to the dangers of epidemics, especially in communities near military encampments. They should be experts in first aid and should have a fundamental knowledge of wartime gases. The civilian population should be taught what to do in such raids. Minutes are important. With lewisite, preventive treatment must be started immediately. By the time a patient reaches a hospital or a decontamination station, it is too late. Civilians must be taught sensible methods, and just as every household is now informed what to do in case of an incendiary bomb, so too each one should be taught the essential measures to be taken immediately in case of a gas attack, for their own protection and for the relief of others. All these directions may be learned from several pamphlets, the most recent

and thorough being the one published by the United States Office of Civilian Defense and entitled *Protection Against Gas*. A can of kerosene, a bottle of hydrogen peroxide and a package of bleaching powder or pail of soapy water, timely and properly used, may save lives.

* * *

A knowledge of dermatology, always important in civilian life, is most essential in industrial and military organizations. Dermatologists have already demonstrated their value in industry. They promoted the Council on Industrial Health of the American Medical Association, pointed out many serious hazards, and suggested methods to prevent them and ways to relieve those affected. The last war taught the value of specialization. In military life, dermatologists should be assigned to their specialty and given an opportunity to teach other medical officers the prevention, diagnosis and treatment of cutaneous diseases. It may not sound very serious to mistake a case of dermatitis due to a hypersensitivity to clothing for a case of scabies or vice versa, but wrong treatment might be serious to the victim as well as to the service when a few days' disability is extended to weeks or months, with great loss of manpower. The training of dermatologists in syphilology should place them in charge of the control and the diagnosis and treatment of this disease. The danger of new and unknown poisons and diseases, against which there is no defense and about which experience alone can teach one, will be ever present in this conflict, so that a constant need of medical literature on these subjects will arise. Hence, the value of continuing medical publications and medical meetings for the dissemination of recent experiences and results is evident. The dangers of the present conflict should be a challenge to the entire medical profession, who should not fear these dangers but should be prepared and willing to share any exposure, hardship or risk to attain the ultimate objective—victory.

520 Commonwealth Avenue

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RETENTION OF A RUBBER TUBE IN THE BILIARY TRACT

Report of a Case

PETER A. CONSALES, M.D.*

BOSTON

THE purpose of this article is to report a case in which a rubber tube was retained for four and a half years in a choledochoduodenostomy communication without any untoward symptoms and with, eventually, the expulsion of the tube and complete restoration of the biliary-duodenal continuity.

CASE REPORT

A 36-year-old married woman was admitted to the Malden Hospital on January 17, 1937, with the complaint of jaundice, itching of the skin and pain in the upper abdomen for the previous 3½ years. There had been marked increase of jaundice, itching and pain for 6 weeks prior to admission. The stools, which heretofore had been clay colored during the attacks and light yellow during the interim, had been clay colored for the preceding weeks.

The patient dated her present complaints to about a year following her first operation, which was performed elsewhere in May, 1932. The gall bladder containing stones was removed, after which there was drainage of bile for 5 months. The wound then healed, and the patient remained in good health for several months. In June, 1933, approximately a year after the cholecystectomy, the upper abdominal pain, jaundice and itching of the skin recurred. The jaundice lasted 2 or 3 weeks and was accompanied by intense pain and itchiness, with clay-colored stools and dark-brown urine. Following each attack, the patient was symptom free for a similar period to relieve her condition, a second operation was performed on October 31, 1933, at another hospital, and a side-to-side choledochoduodenostomy was performed for complete occlusion of the common duct in the second part of its course.

After this operation, the patient was symptom free for about 8 months, when the symptoms of which she previously complained gradually reappeared. At first moderate, the intermittent attacks of pain, jaundice and itching became quite frequent and prolonged on each attack. For 6 weeks before admission, the patient had been quite ill, having had no relief whatsoever. Her skin had become a deeper bronze, and the epigastric discomfort and pain with chills became persistent. At times, the pain, chills, fever and insomnia were so marked and vomiting so severe that the patient had to remain in bed for days. Finally, she sought relief because her condition became progressively worse.

Physical examination revealed a very thin and moderately emaciated woman, markedly jaundiced. The scleras and skin had a deeply bronzed appearance. There were no enlarged lymph nodes. The heart and lungs were essentially normal. The blood pressure was 112/64, the pulse 66, and the respirations 18. The temperature was 98.6°F. The abdomen was rather soft and scaphoid, and revealed a firmly healed incision, about 13 cm. long, below and parallel to the right costal arch. Palpation elicited a definite area of tenderness, moderate muscular spasm

and rigidity above and to the right of the umbilicus. No masses were felt. The liver was very much enlarged and easily palpable, and extended almost to the brim of the right pelvis; the spleen was not enlarged. Many streaked abrasions were present on the arms, legs and body, denoting continuous scratching. Her weight was 121 pounds—39 pounds below her usual weight.

On admission to the hospital, the value for hemoglobin was 80 per cent (Sahli); the red-cell count was 3,500,000, and the white-cell count 9000. The icteric index was 100, as compared with the normal value of 5, and the serum bilirubin (van den Bergh reaction) was 82.5 mg. per 100 cc. The bleeding time was 4½ minutes; clotting began in 5 minutes and was complete in 6 minutes. The blood



FIGURE 1.

This film, taken thirteen weeks after operation, shows extensive filling of the bile ducts and liver radicles immediately following the injection of Hippuran solution through the T tube. Small amounts of the opaque material are visible in the duodenum.

Wassermann reaction was negative. Urine specimens contained a large amount of bile, and the stools were clay colored. A flat x-ray plate of the abdomen revealed no visible calculus in the gall ducts, but the liver was moderately enlarged.

In view of the history and the physical and laboratory findings, a diagnosis of an obstructed choledochoduodenostomy stoma was made, and operation was advised to restore the flow of bile into the intestinal tract. Hypodermoclysis of 500 cc. of 5 per cent glucose twice daily and 15 gr. (1 gm.) of calcium chloride daily were given for 3 days, and on the day prior to operation 475 cc. of citrated blood was given.

*Associate in surgery, St. Elizabeth's Hospital, Brighton

The operation was performed under nitrous oxide, oxygen and ether on January 21, 1937. A Mayo-Robson incision through skin and fascia was carried out; the rectus muscle was divided longitudinally, and the peritoneum opened. Omental adhesions were released from the parietal peritoneum and also from the anterior surface

in Morrison's pouch, and the T tube and drain brought out through a stab wound lateral to the incision. The abdomen was closed in layers, No. 2 chromic catgut being used for the peritoneum and fascia; four stay sutures of silkworm gut were inserted, and the skin was sutured with silkworm gut interruptedly. The operation lasted 85 minutes, and the patient was in excellent condition at its termination. She was given intravenous glucose, and the T tube connected with tubing was brought into a bottle at the side of the bed.

The postoperative course was uneventful. There was slight elevation of temperature for the first 3 days, but the general condition was greatly improved. The appetite was good, the skin took on a lighter hue, and scratching gradually subsided to a minimum degree; the feces, which had taken on a yellowish color 24 hours after the operation, gradually became normal brown in appearance, and the icteric index dropped from 100 to 60. Biliary drainage averaged 100 cc. per day, although the bile was quite viscid at first and very small in quantity; however, with

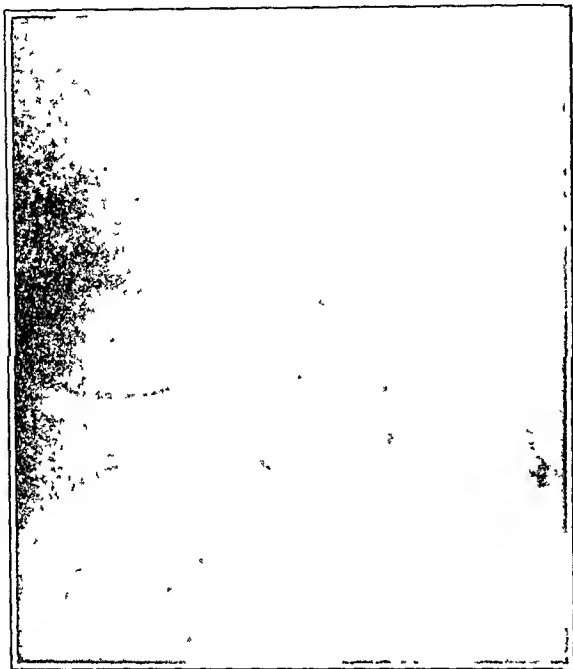


FIGURE 2.

This film, taken five hours after the injection of Hyppuran solution, shows complete disappearance of the opaque material. None of the opaque solution is visible in the intestinal tract. There is air in the duodenum.

of the liver. The liver was greatly enlarged, especially the right lobe, which extended almost to the pelvic brim. Furthermore, omentum adherent to the gall-bladder fossa was released without difficulty, part of the inferior surface of the liver and the first portion of duodenum being brought clearly into view. A bluish discoloration of the biliary duct was readily recognized, and it was evident that the hepatic duct extending 3 cm. downward from the liver was firmly attached at a right angle with the second portion of duodenum. The hepatic duct was then aspirated with a needle and syringe, and clear bile obtained. Further inspection revealed that the hepatic duct was under tension and its walls moderately thick, and that throughout its length—from the inferior surface of the liver to the junction of the duodenum—its width was about 9 mm. Two linen traction sutures were inserted in the wall of the hepatic duct (about 3 mm. apart), and the duct opened through a longitudinal incision. Bile flowed freely, and many small inspissated particles of bile were extracted. Exploration of the duct with a probe, however, revealed that the biliary duodenal stoma was occluded and did not allow the probe to enter the duodenum. The incision of the hepatic duct was then extended through the stoma and into the duodenum, the stoma being thus enlarged. A T tube was then inserted, connecting the hepatic duct with the duodenum. Several interrupted linen sutures were used to approximate the incision and reinforced with a portion of omentum sutured with No. 00 plain catgut. A cigarette drain was inserted



FIGURE 3.

This film shows the horizontal part of the T tube in the biliary duodenal channel; the tube broke at time of removal sixteen weeks after operation. The oval area in the tube indicates where the long arm was cemented.

the administration of bile salts and iron, a definite improvement was noted in the specific gravity of the bile, and the patient regained considerable strength. She was discharged from the hospital on February 6, 16 days after operation. The total hospital stay was 20 days.

At home, temporary clamping of the T tube did not cause any discomfort, and 6 weeks after the operation the tube was finally left clamped at all times. This caused no pain or discomfort, and the stools remained brown. The patient ate about everything without any complaints. On April 21 (13 weeks postoperatively), roentgenographic and fluoroscopic examinations were made by Dr. Max Ritvo (Figs. 1 and 2).

On May 20 (16 weeks postoperatively), under nitrous oxide and oxygen anesthesia, the T tube was removed. In the process of extraction, the long arm of the tube broke off, leaving the T portion of tube in situ (Fig. 3). For a week, bile drained through the skin opening but gradually decreased, and the wound closed 14 days after this mishap. There was no change in the patient's con-



FIGURE 4.

This film, taken four and a half years later, shows absence of tube and depicts liver radicles and duodenum filled with air.

dition, and her stools continued to be brown. She had no digestive disturbances and regained much of her former weight.

X-ray films were then taken at intervals from 6 months to 1 year, and on each occasion the tube was found to be snugly in its original position. On February 7, 1942, however, the tube was no longer present (Fig. 4), and it was evident that the patient had unconsciously expelled the tube. From this, it can safely be said that the tube was in its original place for at least 4½ years. Throughout this period, the patient experienced no untoward symptoms, and for the last year had been working in a laundry.

On her last visit, February 7, she was feeling very well and had no complaints except a sense of fullness in the upper abdomen, especially after a large meal. The stools had been brown, and her weight had remained at 140 pounds. There was no jaundice, the abdominal incision was well healed, and the liver was smooth, 3 fingerbreadths below the costal margin.

DISCUSSION

This case illustrates several interesting points. The first, of course, concerns the reliability of the sidetracking operation of choledochoduodenostomy in stricture of the common duct.¹⁻⁴ That it is not always a successful procedure is well substantiated by men of experience.^{5,6} Others, dissatisfied with

the unsatisfactory results, have resorted to intubation.^{7,8} The varied opinions clearly indicate that these difficult cases are sometimes prone to failure, regardless of procedure. Unquestionably, a prognosis is most difficult to make in such cases.⁹

The second point of interest is that in this case the horizontal part of the T tube broke off at the time of removal, sixteen weeks after its insertion to relieve obstruction following choledochoduodenostomy. Whether this incident was a piece of good fortune is difficult to say. The fact remains that the broken-off horizontal part of the tube remained within the biliary duodenal channel for four and a half years without causing the usual complications of cholangitis and obstruction. Even after the expulsion of the tube, the biliary duodenal communication continued to function very well, although, of course, it is rather soon to venture any prognosis.

This incident does not appear to be the first to be reported. Fedoroff¹⁰ had a similar experience. In his case, the horizontal portion, which broke off at time of removal, was 6 cm. long, and remained within the biliary channel also for four and a half years. When removed, it was found to be covered with *Gallensand*. In Bowen's¹¹ case, it was not the horizontal portion that broke off but the end of a No. 20 Fr. catheter that had been inserted in the common duct; it was 3.8 cm. long and remained in situ for four years.

Possibly the construction of the tubes has some connection with these unusual accidents. Bowen¹¹ insists on the use of a well-made new tube and states that the tubing used should be easily visualized roentgenographically. In the case presented above, the long portion of the T tube was cemented to the short, and for this reason I am fairly well convinced that the construction and, perhaps, the age of the tube were in some measure responsible. Since this mishap, whenever the occasion arose to use a T tube, I have made sure that it was a single piece and never used before.

The final point of interest is that unintentional intubation resulted and the tube was retained for four and a half years without the usual complications. Rubber tubes within the biliary channel have been known to be retained for prolonged periods, even up to many years. The longest recorded period is twelve years¹²; the interior of the tube became encrusted with bile-pigment debris, which obstructed it. Lahey¹³ cites a case in which he removed from the common duct a tube that had functioned well for seven years and replaced it with another. At the time of his report, the second tube was still functioning satisfactorily. Behrend¹⁴ reports a case in which a straight tube

was inserted and the common duct repaired over it for reconstruction of the duct. When the tube was removed six years later, it was encrusted with bile salts. Hunt¹⁵ likewise reports a case in which a tube remained in the hepaticoduodenostomy stoma five months and ten days. He also mentions the fact that he saw an autopsy specimen in which such a tube had remained in place for eight years. Colp,⁷ in presenting his intubation method, refers to a case reported by Judd in which the tube remained in place for four years before it caused cholangitis.

I am fully aware that there are just as many interesting cases in the literature that I was unable to ferret for the simple reason that most of the cases in which a rubber tube was retained for a prolonged period have been solitary experiences and casually mentioned by the authors.

SUMMARY

Choledochoduodenostomy is occasionally prone to failure and fraught with serious complications and experiences.

A case is presented in which the horizontal part of a T tube broke off at the time of removal and became an indwelling rubber tube. It was retained within the biliary duodenal anastomosis without any complications for four and a half years.

In such operations, the use of a new T tube, constructed in one single piece, is recommended.
122 Commonwealth Avenue

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THE CLINICAL APPLICATION OF GASTROSCOPY*

CHARLES W. MCCLURE, M.D.,† AND I. R. JANKELSON, M.D.‡

BOSTON

THE semiflexible gastroscope was introduced ten years ago; as a result, gastroscopy became a relatively simple technical procedure. In the hands of an experienced examiner, it has proved to be a safe method of visualization of the gastric mucosa. Illustrating its increasing popularity is the fact that about four hundred and fifty semiflexible gastroscopes are now in use in this country. Most of these are of German make, but an American-made gastroscope has recently been introduced, and its satisfactory performance is vouched for by Schindler and others who have used it.

The proper evaluation of a new method of diagnosis at best takes time and the collective efforts of the medical profession. Such efforts include those of the enthusiastic pioneer and specialist,

who can compare the objective findings by a new technic with those of the older and well-established methods. However, the clinical status of a new procedure is ultimately decided by the rank and file of the profession, who learn from experience whether this method helps them in their medical practice. These observations furnish the plan that has governed our investigation of the clinical value of gastroscopy. This investigation was incident to the search for methods to increase our diagnostic acumen and persistently carried on in the Gastrointestinal Clinic of the Out-Patient Department of the Boston City Hospital. So far, we have performed over 1500 gastroscopies on patients for whose clinical diagnosis we were responsible. Thus, we have been familiar with their entire clinical record, including x-ray and other special findings. It is on the basis of these observations that we present our conclusions concerning the clinical value of gastroscopy.

In the evaluation of gastroscopy as a method for objectively demonstrating intragastric disease,

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From the Gastrointestinal Clinic, Out Patient Department, Boston City Hospital.

†Assistant professor of medicine, Boston University School of Medicine, junior visiting physician, Boston City Hospital.

‡Assistant professor of medicine, Tufts College Medical School, junior visiting physician, Boston City Hospital.

it is well to compare its relation to roentgenology of the stomach. The two diagnostic procedures are complementary, and are neither competitive nor antagonistic. With the judicious use of both, the error in gastric diagnosis can be reduced considerably.

In our clinical study of the patient, we first obtain a careful history and make a complete physical examination and indicated laboratory tests. Barium x-ray observations are next made for general orientation of digestive-tract disturbances and is an aid in excluding conditions that may contraindicate gastroscopy. After these examinations, the use of gastroscopy is given consideration for two reasons: in the presence of a gastric lesion demonstrated by x-ray study, direct inspection through the gastroscope may furnish evidence enabling a much more exact differential diagnosis; and gastroscopic inspection may disclose an intragastric lesion that the x-ray examination failed to demonstrate. These practical applications of gastroscopy will be clarified by a description of its use in four intragastric lesions. Lack of space precludes the discussion of fissure, superficial ulceration, hemorrhagic areas, diverticulum, petechiae, sarcoma, lymphoblastoma and gumma, or of observations on postoperative cases.

Of the four important intragastric lesions, chronic gastritis is by far the most frequent. The incidence of chronic gastritis is given as 42 to 44 per cent of all cases examined (Schindler,¹ Carey² and McClure, Sweetser and Jankelson³). In a previous communication,⁴ however, we have emphasized that, in approximately 50 per cent of the cases, the gastritis is secondary either to another intragastric or to extragastric disease. By making this statement, we do not choose to commit ourselves regarding whether a chronic gastritis precedes an ulcer or cancer of the stomach or is the result of a pre-existing lesion. This is another chapter whose discussion would lead us far astray from the original purpose of this contribution. What we imply with the term secondary chronic gastritis is the presence of other lesions within the stomach or elsewhere in the body, frequently associated with inflammatory or noninflammatory changes in the gastric mucosa.

Chronic gastritis may be hypertrophic, atrophic, superficial or mixed, and its distribution may be localized or diffuse. In its clinical course, it may simulate a peptic ulcer or be mistakenly diagnosed as a gastric neurosis. Although the clinical diagnosis of chronic gastritis may be suspected, it cannot be made with certainty, and the different types cannot be recognized. The changes in gastric secretions are not diagnostic, and the demonstration

of an excess of mucus in the gastric contents, as well as the presence of leukocytes, is not conclusive evidence. Generally, the clinical laboratory gives indefinite information in this disease. The atrophic and superficial types cannot be demonstrated by either fluoroscopy or x-ray study. The frequently seen large rugae within the stomach are not necessarily due to hypertrophic gastritis (Berg⁵ and Ansprenger and Kirklin⁶). Thus, the roentgen rays are not diagnostic. The only clinical method for ascertaining the presence, type and distribution of gastritis is gastroscopy. The use of gastroscopy for this purpose has impressed us with the fact that minor variations in the appearance of the gastric mucosa as seen through the gastroscope should not be emphasized and that only gross variations from normal are of diagnostic significance. More recently, Swalm and Morrison,⁷ in a gastroscopic study accompanied by biopsies and microscopic examinations of specimens of the gastric mucosa, came to the same conclusions. Their microscopic studies showed a high percentage of verification of the gross picture of chronic gastritis in the cases in which the changes were marked, whereas in the minor variations the error was much greater. Thus, one may say that the diagnosis of chronic gastritis is largely made on the basis of gastroscopic findings. Very similarly, lesions that often accompany a chronic gastritis, such as fissures, submucous hemorrhages, petechiae and small inflammatory polyps, can be recognized clinically only with the aid of a gastroscope. Without it, these lesions may be suspected, but a definite diagnosis is impossible.

The second lesion, peptic ulcer, may be diagnosed clinically if a typical history is obtained. However, an ulcerative gastritis, an ulcerating carcinoma of the stomach or multiple fissures of the stomach may mimic a peptic ulcer to an extent that a differentiation becomes clinically impossible. Moreover, the localization of an ulcer is impossible on the basis of history, physical examination or clinical laboratory data. We need not discuss the necessity of differentiating a gastric ulcer from a duodenal one. Suffice it to say that the former is potentially a cancer, whereas the latter almost never becomes carcinomatous. Hence, every clinical diagnosis of peptic ulcer or a serious suspicion of one requires verification and localization with the aid of a barium meal and fluoroscopic and roentgenographic studies. Thus, the majority of ulcers are located, their sizes and depths determined, their progress evaluated, most of the complications discovered, and the indications for surgery confirmed. However, many ulcers within the stomach are so situated or so superficial that

they cannot be visualized by roentgen rays; frequently, these can be seen by gastroscopy. Furthermore, one cannot determine whether some ulcerative lesions are benign or malignant on roentgenologic evidence, even if the examination is repeated at frequent intervals. However, the gastroscope frequently contributes information that permits the proper classification of such lesions.⁸ In the gastroscopic examination, not only the appearance of the ulcer but also the character of the gastric mucosa of the rest of the stomach may give evidence of the character of the lesion. For example, in the vast majority of benign ulcers, the gastric mucosa appears normal or hypertrophic changes are present, in carcinoma, almost invariably, the entire gastric mucosa is atrophic, whereas in an ulcer that has undergone malignant degeneration only the adjoining mucosa is atrophic.⁹

Although healing of an ulcer can be demonstrated by roentgen rays, at times this evidence is misleading because the niche may appear smaller or less penetrating as a result of exudate accumulated on its base and not due to repair. Such a condition is demonstrable by gastroscopy, which in our experience has proved itself superior to roentgen rays in following the progress of the healing. With the aid of preoperative and postoperative gastroscopy, one makes observations pointing to a major factor in the prevention of the late postoperative gastritis that may accompany peptic ulcer. Our studies indicate that the ultimate results in ulcer surgery are better if the operation is performed at a time when an accompanying gastritis is properly controlled than when it is active. On the other hand, a gastric ulcer not visualized on gastroscopy may occasionally be demonstrated by radiography; therefore, the inability to see an ulcer by gastroscopy does not exclude its presence.¹⁰ Thus, the use of both methods is strongly advocated to reduce the error of diagnosis.

The diagnosis of the third lesion, carcinoma, is usually easy in advanced cases. The appearance of the patient, rapid loss of weight, epigastric distress and anorexia make one suspect it whether or not a palpable mass is present in the epigastrium. Almost invariably, the tumor mass can be located and its extent determined roentgenologically. In other words, only very rarely do the roentgen rays fail to visualize an irregular, moth-eaten deformity of the stomach. However, in a few cases of extensive carcinoma of the stomach, usually involving the posterior wall or the cardiac end, the routine x-ray examination is either inconclusive or negative. In such cases, gastroscopy is indicated and often solves the diagnostic problem. In our experience, gastroscopy is of great help in determining the extent of involvement of the stom-

ach. On the other hand, gastroscopy gives no information concerning regional lymph-node involvement or distal metastases and therefore does not in itself settle the question of operability. Obviously, resectability can be determined clinically only by employment of all methods of examination at one's disposal, including peritoneoscopy.

The early diagnosis of cancer of the stomach is often difficult. The condition is only suspected clinically, and because of the value of an early diagnosis all methods of clinical investigation should be utilized. Roentgen rays and gastroscopy are the two major methods of arriving at an objective diagnosis. If the lesion involves either gastric orifice, the x-ray evidence is usually conclusive. But when the early carcinomatous lesion is away from the cardiac or pyloric orifice, gastroscopy, at least in our experience, frequently becomes essential in the making of a definite diagnosis.

The fourth group of lesions, benign tumors, usually comprise polyps and leiomyomas. The former originate from the mucosa, protrude into the cavity of the stomach, vary in size from a pea to a walnut, and may be single or multiple. A generalized polyposis of the stomach also occurs. The seriousness of polyps lies in the fact that they may ulcerate and bleed and that more than 40 per cent undergo malignant degeneration. Although the larger ones can be demonstrated roentgenologically, the smaller ones may escape detection; thus the radiographic demonstration of gastric polyps is uncertain. Gastroscopically, however, the polyps can be seen, their number determined, their size estimated, ulcerations or bleeding points demonstrated and areas of early malignant degeneration often observed.

The leiomyomas spring from the muscle layers of the stomach, usually in the cardiac end, and may appear as submucosal or subserosal tumors, covered with normal mucous membrane. They too may bleed when they ulcerate and show a tendency to sarcomatous degeneration. Since these lesions are covered by normal mucosa, their character cannot be determined by gastroscopy. Particularly, the subserosal ones, cannot be seen through the gastroscope. The roentgen rays, however, most frequently give information of their location, size and character. These observations emphasize the desirability of both methods in gastric diagnosis.

Whereas other methods, such as roentgenology, give objective information not only about the stomach but also about the adjacent organs, such as the esophagus and duodenum, the scope of gastroscopy is much more limited. Only the mucosa of the stomach can be seen by this method of examination. Moreover, even within the gastric cav-

ity, certain areas may not be visualized and thus a localized lesion may be overlooked on gastroscopy. On the other hand, not only is a lesion located through this instrument but also much information about its character, type, extent and distribution is obtained. Primarily, the gastroscopy gives information about the gross pathologic changes.

Gastroscopy has limitations. In carcinoma, the walls of the stomach may become rigidly infiltrated and lose their distensibility, visualization through the gastroscope being prevented. Although lesions involving the entire gastric mucosa, such as diffuse gastritis, lymphoblastoma and polyposis, can hardly be overlooked on gastroscopy, localized lesions—an ulcer or a single polyp—can be missed on a single examination. The dependability of this procedure in the final analysis depends largely on the experience of the examiner. Besides these limitations, there are contraindications to gastroscopy, which should be scrupulously observed, lest unnecessary accidents be encountered and serious injuries produced to the patient. Since we¹¹ have already listed such contraindications to and limitations of gastroscopy, the reader is referred to this previous publication.

* * *

Röntgenology and gastroscopy are complementary methods of diagnosis, and thus are neither competitive nor antagonistic. In other words gastroscopy is an additional method of arriving at a diagnosis in diseases of the stomach. As such, it does not exclude any other form of examination. In our experience, it has proved to

be a useful procedure, which in many cases has given evidence not obtained by any other method of examination and in others has confirmed evidence otherwise recognized or suspected. Judiciously used, gastroscopy has enlarged the scope of diagnostic acumen. For example, it has rehabilitated the concept of chronic gastritis. It has proved to be a useful procedure in the diagnosis of gastric ulcer and cancer, in preoperative and postoperative observations of the gastric mucosa and in the differential diagnosis of gastric ulcer and cancer. In our opinion, gastroscopy furnishes objective findings whose clinical significance should be established in relation to the history, physical examination, laboratory findings, gastrointestinal roentgen ray studies and all other special studies indicated.

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MEDICAL PROGRESS

STILBESTROL

JOHN ROCK, M.D.,* AND MIRIAM F. MENKIN, M.A.†

BOSTON

“STILBOESTROL” was the name given by Dodds, Goldberg, Lawson and Robinson¹ in 1938 to the compound, 4:4'-dihydroxystilbene, which they prepared from an extract of the oil of aniseed, and which they discovered to be estrogenic. The diethyl derivative (4:4'-dihydroxy- $\alpha\beta$ -diethylstilbene) of this synthesized vegetable hydrocarbon, however, has been found to be so much stronger in estrogenic effect as to make stilbestrol itself clinically unimportant.

GENERAL CONSIDERATIONS

Nature of Drug

The precise Council on Pharmacy and Chemistry of the American Medical Association² prefers to limit the name “stilbestrol” to Dodds's original simpler and weaker estrogen (4:4'-dihydroxystilbene) and uses the rather cumbersome descriptive name “diethylstilbestrol” for the more potent derivative now in such general use as practically to exclude the weak mother substance. In this paper, stilbestrol is employed to designate the drug in common use, 4:4'-dihydroxy- $\alpha\beta$ -diethylstilbene.

Whether used in tablets, in suspensions or in solutions, or whether given by mouth, by injection or implantation, by way of the vagina or percutaneously, stilbestrol, although it is not a true hormone, appears to have all the clinical estrogenic power of the female sex hormone, estradiol, and its various derivatives.³⁻⁶ Whereas Greene⁶ rates 1 mg. of stilbestrol as equivalent to about 20,000 I.U. (international units), or 2 mg., of estrone when both are given parenterally, the same effect is produced by only 0.3 to 0.4 mg. of estradiol benzoate similarly administered. Stoddard and Metzger⁷ report that in the human subject 0.42 mg. of estradiol benzoate, injected intramuscularly, is equaled by 0.5 mg. of stilbestrol taken orally.

The distinct advantage of stilbestrol over estradiol, clinically the most potent of the estrogens, is thus evident. Whereas estradiol loses most of

its efficacy when taken orally, stilbestrol is almost as potent by mouth as by injection.

Cost

A second decided advantage of stilbestrol over estradiol is its lower cost. On the basis of human assay, the result produced by the intramuscular injection of 0.42 mg. of estradiol benzoate, priced at \$1.07, may be duplicated by the oral consumption of 0.5 mg. of stilbestrol, costing less than 2 cents.⁷

Pharmaceutical Forms

The drug is dispensed in small tablets, some of which are enteric coated, as well as in capsules and suppositories. Soon, no doubt, it will be obtainable in solutions or suspensions for percutaneous use, as well as in pellets that can be implanted, since these forms have been successfully employed in clinical experimentation.^{8,9} It is questionable, however, whether these will ever be of great value, since stilbestrol is so effective by mouth.

Dosage

The effective dose of stilbestrol varies considerably because patients have widely different susceptibilities, both to desired and undesired results, and because among the many disorders that it may relieve, some are easily affected, whereas others are very resistant. Since the drug may have unpleasant sequelae, as mentioned below, it is wise to begin treatment with as little as 0.1 mg. by mouth daily. If well tolerated, this may be increased even up to 5 mg. daily, although only occasionally is it necessary to exceed 1 mg., and only rarely, as for the suppression of lactation, is one obliged to give more than 2 mg. daily. When injected, it should be put in muscle, and then only on every third or fourth day; the gluteus medius on alternate sides is very suitable.

Utilization

Stilbestrol is effectively absorbed from both the intestines and the muscles but is not utilized in the same degree from these two sources. On the basis of analyses made on 3 menopausal patients, von Haam et al.¹⁰ estimated that 10 to 30 per cent of a single large dose of injected stilbestrol was ex-

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, Vol. III, 1942* (Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

*Instructor in gynecology, Harvard Medical School; visiting surgeon, Free Hospital for Women.

†Research associate, Free Hospital for Women.

reted in the urine and feces during the first ten days after its administration. Zondek¹¹ reported that one fourth of the amount injected into infantile rats could be recovered from the excreta. He also found that, forty-eight hours after injection, stilbestrol could be recovered by extraction only from that half of the animal in which it had been injected. There is therefore "storage" at the site of injection. The limits of storage after implantation of pellets were suggested by Forbes,¹² who stated that 90 per cent was absorbed in the rat in fifty-one days.

Toxicity

The dosage is properly limited to that which gives the desired effect, but also by possible gastrointestinal disturbances, and occasionally by less common sequelae, such as those noted in the literature by Morrell.¹³ These include headache, drowsiness, vertigo and dermatoses. Von Haam et al.¹⁰ mention excessively increased libido. We have not been informed of anything approaching this by our patients; nor indeed, except rarely, have we found it to increase sex drive at all. Physicians were made unduly apprehensive of the toxicity of stilbestrol by some early investigators, who, accustomed to the mild estrogenic effects of some of the hormones, used what proved to be unnecessarily large doses. The long delay in approval by the Food and Drug Administration, while it very properly gathered large numbers of reassuring reports,^{6, 13-16} contributed to the uncertainty among clinicians.

Our experience regarding toxic reactions is much the same as those cited. We find that such symptoms as nausea, vomiting, headache and malaise were encountered in 31 of 199 patients (15.6 per cent) treated for various complaints, chief among which were menopausal symptoms and menstrual disorders.* Toxicity depends on individual sensitivity as well as on dosage. The menopausal patients appear to be less susceptible than those treated for menstrual disorders. Toxic symptoms were reported in only 12.4 per cent of the former, as compared with 23.1 per cent of the latter.† Pregnant or lactating women are said to tolerate tremendous amounts^{8, 11, 17, 18} Zondek and Bromberg¹⁰ mention a patient who could take one hundred and seventy times as much stilbestrol when pregnant as when not pregnant; they concluded that there was a detoxication of the material during pregnancy. Toxic reactions are not confined to stilbestrol, but may be elicited also by overdosage

with any of the hormonal estrogens.⁶ There seems to be no evidence of serious liver, kidney or bone-marrow damage, such as was feared following the earliest reports,^{13-16, 20} when unsuspectingly excessive doses were used. Transient nausea is the commonest of the infrequent objections to the drug. We have satisfactorily avoided this by instructions to take the tablet at bedtime, because the disagreeable symptoms usually follow only a few hours after ingestion. Abarbanel and Klein⁸ find that bile salts or acid preparations help in preventing these effects. Others¹ believe that the enteric-coated pill is less troublesome.

Finch²² regards these untoward symptoms as an allergic response and reports desensitization to the drug by frequent medication, beginning with a low dosage and gradually increasing this until the therapeutic level is reached. An allergic reaction to stilbestrol had previously been noted by Baird.²³

Hamblen²⁴ expresses perhaps the greatest danger in the use of nonhormonal estrogens. "Being orally active, cheap and highly potent, uncritical use of them by physicians and self medication with them by patients would add, doubtlessly, to an already widespread contraphysiologic and empiric estrogenic therapy."

Carcinogenic Effect

Much loose thinking has prevailed regarding the carcinogenic properties of the estrogens, among the most potent of which one must place stilbestrol. Since its effect on the uterus and breast is similar to that produced by various natural estrogens, it seems more than likely that its potentiality to develop cancer is the same. But for cancer to develop, the unknown cancer factor is generally considered essential. On the other hand, once the cancer factor is activated by the intrinsic growth potential or by artificial growth stimulus, such as Gardner et al.²⁵ gave in the form of estrogen to male mice of a cancer strain, the tumor may then progress, even if the artificial stimulus is discontinued. Removal of an endogenous agent sometimes effectively halts the growth. This has been seen after castration in some cases of metastatic cancer of the breast, and also of cancer of the prostate. The great majority of experimental efforts to initiate cancer in various species, even including the monkey, have failed. Zondek¹¹ has mentioned several investigative attempts, some apparently successful, and also reported his failure to induce cancer by giving tremendous doses of estrogen over many months to members of his strain of rats, among 5000 of which no spontaneous cancer had ever been found. He recorded Engle and Smith's failure to produce

*This study was carried on at the Free Hospital for Women, Brookline, Massachusetts, with material generously supplied by the Winkrop Chemical Company Incorporated, New York City.

†The previously quoted figure 15.6 per cent refers to the incidence of toxic symptoms in a group of 199 cases which also included other conditions such as . . .

cancer in 4 macaques and also Zuckerman's inability to cause cancer in monkeys by large doses of estrone over long periods. Zuckerman treated monkeys for a year with a total of 365,000 I.U. of estrone. Because 2 women, both of whom had received 50,000 I.U. of estradiol benzoate daily for twenty-four days, or a total of 1,200,000 I.U., showed no carcinoma, Zondek concluded that even extremely large doses of hormone did not cause carcinomatous changes of the uterus. He believes that large doses may even protect against the initiation of cancer because of the consequent inhibition of the growth effect of the anterior pituitary gland, as well as by the resultant hormonal castration. In 195 patients who received appreciable amounts, we have seen no cancer develop during the exhibition of stilbestrol or soon after its consumption. Because of the nature of estrogen metabolism, long-delayed effects of its use are not to be apprehended. This does not mean that cancer need not be kept constantly in mind, for it can develop in any female at any age. However, we do not subscribe to the notion that any estrogen per se is carcinogenic.

CLINICAL USE

Primary Amenorrhea

Stilbestrol, like the natural estrogens, is unpredictable as a precipitant of bleeding in cases of primary amenorrhea but, if given for two or more weeks, usually produces flow, either during the treatment or as a withdrawal phenomenon. The dose need not exceed 2 mg. daily; Palmer²⁶ used seven daily doses of 1 mg. each, followed by seven daily doses of 5 mg. Doses larger than 2 mg. may elicit unpleasant nausea or tenderness of the breasts. In susceptible persons, however, toxic symptoms may follow the exhibition of only 0.1 mg. daily. If a clinical *tour de force* is sought because of the temporary psychologic "lift" that a period of flow gives the defective girl, it may be more surely obtained by the simultaneous ingestion of 2 mg. of stilbestrol and the intramuscular injection of 5 to 10 mg. of progesterone on five successive days.

Secondary Amenorrhea

In the girl or woman whose germinal epithelium is active, but who has merely stopped maturing follicles, stilbestrol is much more useful. One milligram daily by mouth for fourteen to twenty-one days is almost certain to be followed, within four to ten days, by a flow that satisfies the patient. In a very few cases, a second spontaneous flow follows some weeks after treatment. If a succeeding series of treatments is started at the time of the bleeding, the flow is usually repeated. This may be

kept up for months, but the likelihood of spontaneous recovery of the ability to ovulate is not thereby enhanced; we have observed, however, that it is not always destroyed.

Aperiodomenorrhea (Immeasurable or Anovulatory Menstruation, Uterine Dysfunction)

When flowing is irregular in incidence or prolonged, and sometimes when it is profuse, it may be brought to a semblance of normality again by repeated cyclic series of stilbestrol treatments, consisting of 0.5 to 1.5 mg. daily for arbitrarily selected periods of fourteen to twenty-one days. Succeeding periods of treatment are started with or soon after each period of flowing.

Menopausal Symptoms Incident to Normal or Artificial Climacteric

The greatest value of stilbestrol is in the treatment of these conditions. Initial dosage is properly about 1 mg. daily. When comparative comfort has been re-established, the dose should be diminished to the individually critical level, which may seem ridiculously low; occasionally, it can be increased without causing toxic symptoms. Natural remissions in the first ten years of the normal menopause are not infrequent, and at such times, medication should be reduced or omitted. Intermittent administration of any estrogen is necessary to relieve the anterior pituitary gland of undue inhibitory influences. There is as yet no reason to suppose that the carefully graded use of any estrogen during the menopause merely postpones the evil day when the unpleasant subjective symptoms must be suffered before stabilization is accomplished. Rather, it seems that final comfort without medication can be gradually attained by the use of smaller and smaller doses of an estrogen; and stilbestrol is a good one.

Of great significance during and after the menopause is the fact that stilbestrol stimulates proliferation of the endometrium and establishes therein the potentiality to bleed, and that this potentiality may be activated during treatment and will surely express itself after cessation of the drug, if it has been used for several weeks. This phenomenon is important mainly because it may not disturb the unwary clinician as much as it does the apprehensive patient. The first bleeding from cancer of any part of the uterus must not be overlooked. Careful examination and continued close observation for long periods after omission of the drug are essential.

Suppression of Lactation

We have not used stilbestrol to inhibit lactation. Davis and Boynton¹⁵ report that if treatment with 5 mg. for eight to ten days is started promptly on

delivery, no engorgement occurs. If, on the other hand, the drug is withheld until after lactation is established, they state that the engorgement of weaning, although it does take place, is usually slight. Abarbanel and Klein⁸ found that stilbestrol in doses up to 500 mg. did not affect established lactation in the nursing woman. Mendel, Goldman and Caire²⁷ noted primary suppression of lactation in 98 per cent of 55 patients. Many other workers^{8, 17, 18} present similar results, and all mention the extreme infrequency of any unpleasant symptoms, even though such large doses are given as would certainly be toxic to the nonpuerperal patient.¹⁹ Abarbanel and Klein⁸ gave doses ranging from 250 mg. a day to 1500 mg. a week to pregnant and puerperal patients, and recorded no toxic effects except occasional dizziness.

Dysmenorrhea

For dysmenorrhea, a very common gynecologic disorder, estrogens, stilbestrol among them, have a very limited field, because to relieve the pain they must prevent ovulation. Thus, to upset what is frequently a delicately balanced mechanism in any girl is usually too high a price to pay. Sturgis²⁸ is right when he says that if 1 mg. of stilbestrol is given daily for twenty days, beginning a full week before the expected time of ovulation, the succeeding period of flow will be painless. He finds, furthermore, that the omission of treatment in the succeeding cycle permits the re-establishment of ovulation. Therefore, the procedure may occasionally be justified in the rare patient who apprehends that pain will materially interfere with some important performance—artistic, athletic, social or academic. Frequent or prolonged use of this method might seriously upset the endocrine balance that is necessary for normal cyclic ovulation.

Senile Vaginitis

In postmenopausal vaginitis, suppositories containing 0.5 to 1 mg. of the drug used daily for several weeks will rejuvenate the vaginal epithelium and re-establish its high resistance to the commoner bacterial and fungoid irritants. Davis and Boynton¹⁵ recommend the use of a 0.5 mg. suppository each evening for six to eight weeks; we have noted alleviation of the condition in less time. Abarbanel and Klein⁸ effectively used a stilbestrol ointment for this purpose, and also suggested stilbestrol in suppositories for gonorrheal vulvovaginitis in children, a condition with which we have had no experience.

Pruritus Vulvae

As an adjuvant in the relief of vulvar itch, which is often very distressful, stilbestrol by mouth in

doses of 0.5 or 1 mg. daily, or by inunction, as reported by Abarbanel and Klein,⁸ by Wharton²⁹ and by Lubow,³⁰ may be very helpful, but other measures should also be taken. The urine must be sugar free. The application of 2 per cent boric acid helps to eradicate the almost constant bacterial dermatitis, and painting with gentian violet usually removes the commonly found fungus.

As already mentioned in connection with the menopause, stilbestrol may also evoke bleeding in the aged if given for several consecutive weeks. When it does so, the treatment must be stopped, and any recurrence should be regarded as indicating cancer until thorough search by curet and biopsy reveals no such growth.

* * *

Stilbestrol, a potent synthetic estrogen, is marketed in various forms, since it is effective orally, intramuscularly or percutaneously, and bids fair to supplant the natural estrogens in therapeutics. The standard daily dose is considered to be 0.1 to 1 mg., although some patients profitably take as much as 5 mg. Overdosage or undue susceptibility is associated with nausea and occasionally with various other symptoms of mild toxicity, but there is no evidence that the drug is dangerous. It has been reported that desensitization is possible by the use of gradually increasing doses. During pregnancy and lactation, tolerance is tremendously raised.

Like other estrogens, stilbestrol seems not to be carcinogenic per se, but it does cause proliferation in the epithelium of the reproductive system.

Its greatest usefulness is in the treatment of menopausal symptoms and in the production of flow in the amenorrheic patient. It may occasionally be used for the relief of dysmenorrhea, provided that treatment is started at least one week before ovulation time, so that follicular rupture is prevented.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28411

PRESENTATION OF CASE

A fifty-two-year-old married woman was admitted to the hospital because of pain in the chest.

Ten months prior to admission, the patient noticed transient pain in the chest beneath the left breast. This was not severe but was worse on inspiration. Soon after this, she developed exertional dyspnea and often wheezed. She was treated by her physician for a "heart condition," and digitalis was administered. Following this, all symptoms were relieved. Six weeks before entry, the patient developed a little pain under the upper portion of the left shoulder blade and occasional pains in the left shoulder. At about this time, she noticed that the left upper chest seemed "full" and that the veins over the chest were prominent. She believed that she had lost a little weight.

The family and past histories were irrelevant. A brother had died of cancer of the rectum.

Physical examination revealed a nervous, well-developed and well-nourished woman in no distress. The pupils were equal in size. Examination of the heart and right lung was negative. The left upper chest seemed fuller than the right. The veins over this side appeared prominent. The amplitude of inspiratory and particularly expiratory movements was reduced. The anterior and posterior aspects of the upper left chest were flat to percussion. Tactile fremitus and breath sounds were diminished above the fifth rib anteriorly and the eighth rib posteriorly. There was a fullness of the left supraclavicular fossa, which seemed to extend beneath the clavicle. The left hand was warm and dry; the right was cool and wet. Abdominal examination was negative.

The blood pressure in the left arm was 152 systolic, 82 diastolic, and in the right arm, 138 systolic, 80 diastolic. The temperature was 98.1°F., the pulse 78, and the respirations 20.

Examination of the blood revealed a hemoglobin of 14.5 gm. and a white-cell count of 8100 with 81 per cent polymorphonuclears. The urine was acid in reaction and had a specific gravity of 1.022; the sediment contained 22 white cells and 7 epithelial cells per high-power field. An electrocardiogram demonstrated a normal sinus rhythm

of 65. There was a tendency toward right-axis deviation, but the record was within the normal range. T₁ was flat to very slightly diphasic; T₄ was flat to very slightly inverted. The blood Hinton test was negative.

An x-ray film of the chest revealed a dense homogeneous mass that filled the left pleural cavity from the apex to the eleventh rib (Fig. 1). The lower margin of the mass was lobulated. The mediastinum and heart were displaced markedly to the right. The lung between the lower limits of the mass and the left diaphragm appeared to be bright, probably owing to emphysema. The right lung field was clear, and there was an azygos lobe. There was no definite evidence of erosion of the ribs or enlargement of the intervertebral foramina. The patient was operated on fourteen days after admission.

DIFFERENTIAL DIAGNOSIS

DR. HELEN PITTMAN: May we see the x-ray films?

DR. GEORGE W. HOLMES: Whatever this process is, it has advanced beyond the stage where the radiologist can make a complete diagnosis. The process is homogeneous throughout on the routine film. On a film taken with a Bucky diaphragm, this finding was confirmed. Consolidation with cavity formation might look like this, on the first film, but not like that, on the second; so we can be fairly certain that the lesion had a fairly homogeneous density throughout. The heart and mediastinal contents are displaced away from the lesion. That is evidence of some space-filling lesion, such as fluid or tumor, rather than collapse. The fact that the lower part of the lung field is clear is against a large accumulation of fluid in the pleural space. The fact that it bulges might be interpreted as due to fluid or tumor. The absence of erosion of the ribs or bodies of the vertebrae is against a tumor's arising from the sympathetic chains or the spinal nerve roots,—the neurofibroma group,—but it is not against a primary lung tumor. The fact that the other lung is clear is against a tuberculous lesion. I think the evidence we have here rather points toward neoplasm; whether it was primary or secondary, we have no definite evidence.

DR. PITTMAN: We are obviously faced here with a tumor of the mediastinum, and how much farther than that I can go I am not at all sure. I can do a certain amount of reasoning and a larger amount of guesswork, and end up with "tumor of the mediastinum, type to be determined later on."

We have a fifty-two-year-old woman, who was not sick, who may have lost weight, but who was still well nourished, and who had no fever or leukocytosis. Ten months before entry, she began to have pain. Then she was well for eight months but, by the time of entry, was having more symptoms. The only symptoms that she had had are

sympathetic system, demonstrated by the fact that her hands showed different temperatures and different degrees of moisture, and bronchial pressure, indicated by lack of aeration except at the base, where there appeared to be some emphysema.

I am not going to inflict on you a complete differential diagnosis of tumors of this region of the

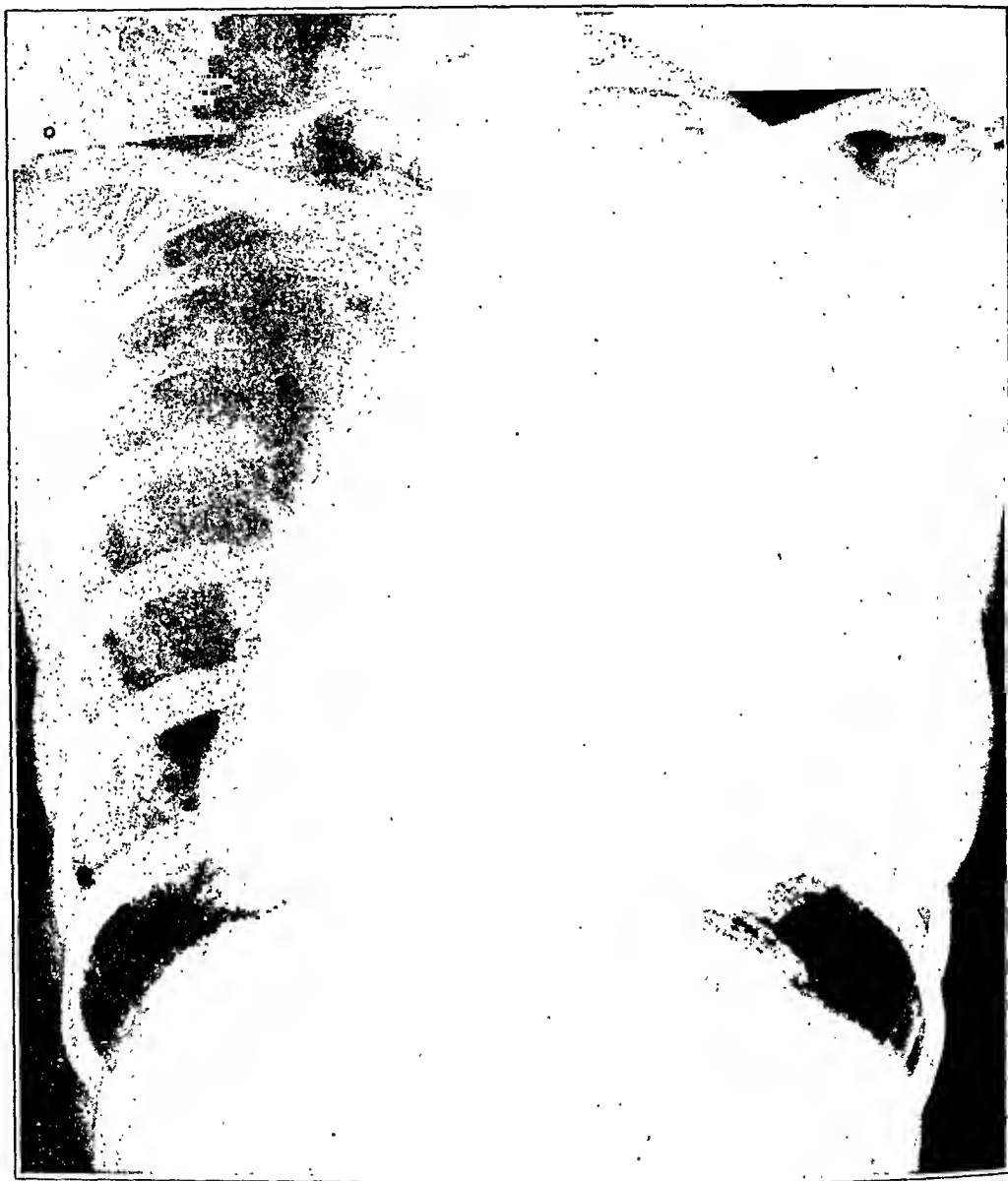


FIGURE 1. *Anteroposterior Film of the Chest.*

those that I attribute to pressure. True, the pain that she had at the beginning in her left breast and the pain later in the left shoulder may have been pleural and not due to pressure. A few things here I think are a little queer. If not queer, I just do not understand them. She had a large mass in the left chest bulging above the clavicle. Vascular compression was evidenced by dilated veins, and yet the blood pressure on that side was higher than on the other side. I have no idea how or why that occurred. She also had pressure on the

body. I think there are three things to be considered.

The first one I thought of, as I read over the record and before I had seen the x-ray films, was aneurysm, and we still must consider aneurysm of the descending aorta; such lesions are relatively symptomless and likely to be silent until they have attained considerable size and are then picked up because of pressure symptoms. This holds true in this woman. On the other hand, with an aneurysm of this size, I think we should expect to find

ome evidence of erosion of the vertebral bodies or ribs. The blood Hinton test was negative, and we had equal pupils. I do not believe we have enough evidence here to make a diagnosis of aneurysm.

Then we come to new growths in this region, and a solid malignant tumor is a possibility. I believe sarcoma is far and away the commonest. This patient had a very large lesion without any evidence, so far as we are told, of metastatic disease. It seems hard to me to consider sarcoma as large as this with no evidence of the same disease elsewhere in the body, and in a woman who is not sick. Lymphoma can never be excluded. One always has to mention it. Very much the same argument holds as in sarcoma. The only temperature report is a normal one. Again, the woman is not sick, and no mention is made of enlarged lymph nodes. It does not say that she had one, but I am assuming that that information was not intentionally left out, and that none were found.

I have never seen an intrathoracic thyroid gland of all comparable in size with this, and I am just not taking any stock in it. That brings us down to benign tumors of the mediastinum, which are statistically rare. I think, however, that a benign tumor fits in with the situation we have here reasonably well, a very large growth with no symptoms until it caused pressure, and in a woman who was not ill.

A dermoid is always a possibility. The Bucky film certainly shows a uniform density, but unless one can pick up a tooth or bone or something else of different density or unless there is ulceration into the bronchus, one cannot be sure. The patient coughed up no characteristic material. I do not see that we have any right to think we are dealing with a dermoid, particularly since this woman was older than most individuals are when dermoids are found. A lipoma, which could occur in this position, must be seriously considered even though it is not seen very often. I believe fibromas also can arise in this position. They are not seen often, but again they are picked up only because of their pressure symptoms in an essentially healthy person. I have considered this mass as having arisen from the structures of the mediastinum, but I suppose there is no way of being sure it did not arise from either bronchus or lung. We have very little, however, pointing to its origin in a bronchus or the lung, so I am going to stick to the mediastinum as the source. I am therefore left just exactly where I was in the beginning, with a large lump occupying the chest, and I do not know what it is, but I think it is extremely unlikely to be a malignant tumor. I think we have no data on

which to make a diagnosis of aneurysm and I therefore make a diagnosis of benign tumor and suggest that it might have been a lipoma.

DR. TRACY B. MALLORY: Would you expect it to have that degree of density, Dr. Holmes?

DR. HOLMES: No.

DR. MALLORY: A fibroma would fit better with what you see?

DR. HOLMES: Yes.

DR. EDWARD D. CHURCHILL: We made a diagnosis of benign mediastinal tumor. The rest of the problem was a technical and mechanical one. The first consideration, in which we very likely decided incorrectly, was the route of approach. There were two choices. The incision may be placed anterolaterally or posterolaterally. Because of the evidence that the tumor extended above the clavicle, and in anticipation of difficulty in freeing it from the subclavian artery or vein, we chose an anterolateral incision. The operative notes read as follows:

A portion of the seventh rib anteriorly was resected, and the pleural cavity opened. An enormous tumor was found, apparently completely filling the left chest. It was obvious that a wider opening of the chest was necessary. The sixth rib was divided and retracted. This did not give satisfactory exposure, and it was necessary to divide the manubrium, which was done transversely in the region of the sixth costal cartilage. This enabled a hand to be passed up and around the tumor. The lung was found displaced and compressed downward and backward, and apparently was completely atelectatic. The tumor had extended high into the left apex and was adherent to the posterior mediastinum and posterior surface of the left apex of the chest. It was freed up and gradually released. There was profuse bleeding from veins on the inner aspect of the chest wall in the apex. An attempt was made to stop hemorrhage by ligatures and suture. Several sutures were taken in the posteromedial aspect of the collapsed left upper lobe, and this in turn was sutured into the apex. During the procedure, the patient went into shock, apparently owing to blood loss. Two transfusions were given during the operation.

In order to deliver this enormous solid tumor even after making the maximum exposure by resection of ribs, it was necessary to divide the sternum transversely. I had hoped of course that the tumor was cystic and that its size could be reduced by aspiration, but that was impossible because it was a solid tumor. A tumor of this size in the chest does not have a pedicle, like a tumor of the ovary, which can be simply dealt with because, when it is delivered, the pedicle can be secured. This tumor had a broad base on the lateral aspect of the vertebral column and the heads of the ribs.

The patient died of primary hemorrhage because the blood was coming much faster than we could put it in with transfusion. This represents

an error in surgical judgment, since we could not control a situation that we had created. Whether, if I had utilized a posterolateral incision, it would have brought me nearer the lateral aspect of the vertebrae with better opportunity to control the large veins before they were cut or torn, I do not know. If I were doing it again with this experience in mind, I should certainly use a posterolateral approach.

CLINICAL DIAGNOSIS

Mediastinal tumor (? neurofibroma).

DR. PITTMAN'S DIAGNOSIS

Benign tumor of mediastinum (? lipoma).

ANATOMICAL DIAGNOSIS

Fibroma of mediastinum.

PATHOLOGICAL DISCUSSION

DR. MALLORY: From the histologic point of view, this was a fibromatous tumor, evidently very slowly growing and of long duration. It showed small areas of cystic degeneration, though not enough so that an appreciable amount of fluid could have been withdrawn and the mass significantly reduced in size. It was essentially a solid tumor. There were also large foci of xanthomatous degeneration with many cholesterol crystals. Whether it arose from the perineurial sheaths, I cannot say with certainty. It has not the obvious earmarks of perineurial fibroma, but on the other hand, there are areas that do suggest such a diagnosis. Since the majority of tumors in the mediastinum are of neural origin, that would be my guess; but I cannot prove it.

DR. CHURCHILL: There was a definite constriction ring in the tumor representing the first rib and the clavicle. It was hourglass in form where it had extended up above the first rib and had become tightly wedged in place.

DR. MALLORY: There is one discrepancy between your operative findings and the x-ray report. That is the question of air beneath the tumor. Your impression, I believe, was that the lung was entirely collapsed.

DR. CHURCHILL: Undoubtedly the lower portion of the lung contained air.

DR. RALPH ADAMS: Would you expect erosion of the ribs posteriorly in such tumors?

DR. HOLMES: Yes.

DR. CHURCHILL: That was another reason we went in anteriorly.

DR. LERMAN: Can you tell where the blood supply is coming from?

DR. CHURCHILL: Only in retrospect.

DR. JACOB LERMAN: In any type of tumor?

DR. CHURCHILL: Very often it is predictable, as, for example, with an intrathoracic goiter.

CASE 28412

PRESENTATION OF CASE

A thirty-six-year-old married woman was admitted because of pain in the chest.

Approximately three months prior to admission, the patient began to have rather severe aching and, at times, shooting pains in the left side of the chest above the breast. Often, the pain seemed to radiate down the left arm and occasionally to the spine posteriorly. The episodes varied in length from a few minutes to an hour and occasionally awakened the patient during the night. The pain was not related to exertion. During this illness, the patient suffered with infrequent dizzy headaches and was slightly dyspneic. She was able to climb only a single flight of stairs. Occasionally, the dyspnea was relieved by taking soda and belching. During this time, she raised a small amount of pale-yellow sputum without coughing. Two months before entry, x-ray treatment was administered to the chest, following which her symptoms of shortness of breath were relieved and the amount of sputum reduced.

The family history was noncontributory. When twenty-six, the patient had pneumonia, which was complicated with right-sided empyema necessitating rib resection and open drainage; Type 4 pneumococci were recovered from the pus. She made a satisfactory recovery and had no symptom related to the chest until the present trouble.

Physical examination revealed an obese woman in no acute distress. Examination of the heart and lungs was negative except for a few rales audible at the base of the right lung posteriorly. There was a slight amount of tenderness over the entire lower abdomen—the patient stated that she was menstruating.

The blood pressure was 110 systolic, 70 diastolic. The temperature was 99°F., the pulse 77, and the respirations 20.

Examination of the blood revealed a hemoglobin of 14 gm., and a white-cell count of 9500 with 73 per cent polymorphonuclears, 15 per cent lymphocytes, 6 per cent monocytes, 5 per cent eosinophils and 1 per cent basophils. A catheterized specimen of urine was acid in reaction, had a specific gravity of 1.015 and gave a ++ test for albumin; the sediment showed 20 white cells, occasional epithelial cells and many bacteria per high-power field. The blood Hinton reaction was negative. The nonprotein nitrogen was 22 mg. per 100 cc.

An x-ray film of the chest demonstrated an 8-by-5-cm. homogeneous mass attached to the right posterior margin of the trachea from the level of the clavicle downward; the mass displaced the

trachea and esophagus to the left (Fig. 1). The displacement of the esophagus appeared to be due to pressure without evidence of attachment. The mass moved with swallowing. In the lateral view, there appeared to be some narrowing of the trachea in the region of the mass. The fifth and sixth right ribs showed old resection, with partial regeneration of the bone in the posterior axillary line. There was evidence of old pleurisy on the right. The lung fields were clear. The heart appeared normal.

DR. ADAMS: Does the displacement of the

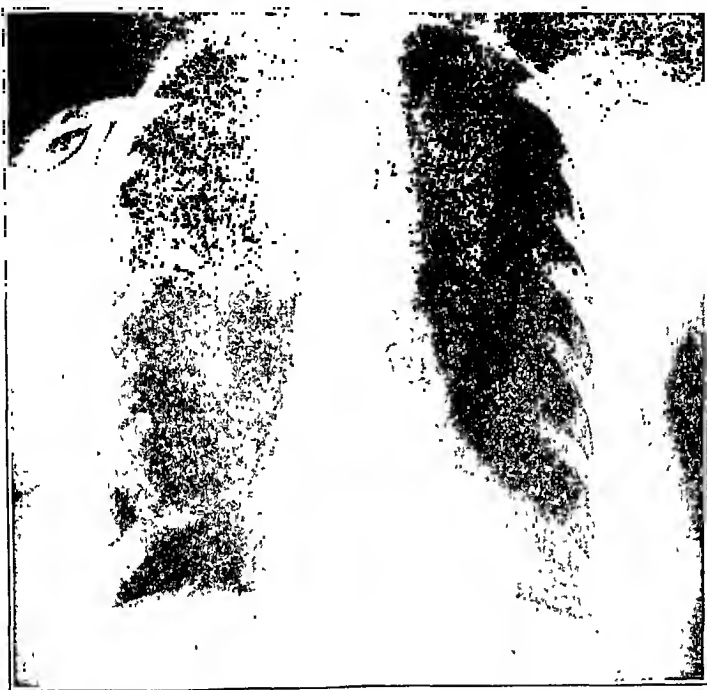


FIGURE 1 *Anteroposterior Film of the Chest.*

trachea and esophagus to the left (Fig. 1). The displacement of the esophagus appeared to be due to pressure without evidence of attachment. The mass moved with swallowing. In the lateral view, there appeared to be some narrowing of the trachea in the region of the mass. The fifth and sixth right ribs showed old resection, with partial regeneration of the bone in the posterior axillary line. There was evidence of old pleurisy on the right. The lung fields were clear. The heart appeared normal.

Eight days after admission to the hospital, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. RALPH ADAMS*: May we see the x-ray films?

DR. GEORGE W. HOLMES: The patient had had part of a rib removed. This is the mass that we are interested in. It shows most clearly in this second film, taken with a Bucky diaphragm to

bring out the outline of the tumor. Here you see the displaced esophagus and trachea. The arch of the aorta is here. The lateral view does not help us.

DR. HOLMES: I think it does.

DR. ADAMS: But does it go up to the level of the thyroid cartilage?

DR. HOLMES: It is questionable whether it does that.

DR. ADAMS: Is the esophagus displaced anteriorly or posteriorly? Or can you tell?

DR. HOLMES: Not from these films, and I do not believe anything is said about it in the notes.

DR. ADAMS: It states in the records, "The displacement of the esophagus appeared to be due to pressure without evidence of attachment." Could you rely on the member of your department who made that statement?

DR. HOLMES: I suspect it was Dr. Richard Schatzki. He has been doing a lot of work on that subject, and I should put considerable weight on what he says. How he finds it out, I do not know.

*Surgeon, Lahey Clinic

DR. ADAMS: The problem in differential diagnosis in this case is to define the type of superior mediastinal tumor that is displacing the esophagus and trachea, causing dyspnea by tracheal compression and producing pain by usurping space at the thoracic inlet, where space is limited. Mediastinal tumors are unsurpassed as stimulators of diagnostic guessing bees, and rarely can the correct guess be supported by critical evidence logically establishing the one diagnosis and definitely excluding all others.

From the history one obtains nonspecific information of both positive and negative value. Radiation of pain to the midclavicular line is observed in many pulmonary and mediastinal lesions, perhaps because anterior cutaneous branches of the intercostal nerves are distributed to that region. The intermittent character of the pain is indicative of an expanding lesion, but expansion can occur in either a cystic or a solid growth. The increasing dyspnea can best be explained by pressure and distortion of the trachea, which was compressed anteroposteriorly and displaced laterally to the left. Other possible explanations, such as heart disease or lung disease, are ruled out by lack of collateral symptoms and physical or x-ray signs of disease in the heart or lungs.

The pale-yellow sputum produced without coughing is puzzling. Most sputum is coughed up. In fact, only sputum lying in the upper trachea and larynx can be raised without coughing. The absence of cough means that there was no irritative lesion of the tracheal or bronchial mucosa, and yet the accumulation of small amounts of pale-yellow sputum, probably mucoid in type, rather than purulent, suggests that there was some mucosal irritation. Extrinsic pressure on the upper trachea could produce this paradoxical situation. Decrease in sputum and dyspnea after x-ray treatment might mean that a malignant tumor, such as lymphoblastoma, had proved sensitive to irradiation, had shrunk in size and had been followed by clinical improvement. It could also mean that the x-ray therapy had merely suppressed secretory function of the tracheal mucosa and that the improvement in dyspnea was coincidental. There is nothing in the clinical summary suggestive of carcinoma of the esophagus or bronchus, that is, no difficulty in swallowing, no food regurgitation, no cough and no hemoptysis: some one of these symptoms would surely be associated with a carcinoma of the bronchus or esophagus casting an x-ray shadow of this size. Also, x-ray films show none of the features to be expected in an invasive lesion of the esophagus or trachea. Cancer will therefore be dropped from further consideration.

It is contrary to usual experience to find a lymphoma of this size localized to one portion of the mediastinum without palpable nodes in the neck, axillas or groins, and with a blood smear so nearly normal. A lymphoma that responded to x-ray treatment with regression in symptoms should have almost disappeared within two months if the treatment was adequate. A tumor of the lymphoblastoma series is therefore believed unlikely.

The history of pneumonia and empyema apparently has no connection with this episode and presumably is included to explain the rib defects and the old pleurisy at the right lung base.

The temperature of 99°F., the white-cell count of 9500 and the polymorphonuclear percentage of 73 indicate slight infection. One possibility is cystitis, because of the report of urine containing albumin and white cells. Another is that the lesion in the chest contained infected material or was surrounded by an inflammatory reaction.

Mediastinal dermoids commonly arise in the anterior portion of the chest, and if they attain sufficient size, most often displace the midline structures posteriorly. This lesion displaced the trachea anteriorly. A dermoid cyst probably is not the answer, although it is ruled out on this point alone. Mediastinal neurofibromas tend to arise in the posterior regions, in proximity to the sympathetic nerves. Consequently they appear in the costovertebral gutter, and before resulting in displacement of the trachea and esophagus, cause erosion of the ribs over which they lie. There is no sign of rib erosion in this case.

Except for the statement that "the displacement of the esophagus appeared to be due to pressure without evidence of attachment," one would consider seriously the diagnosis of a benign tumor of the esophageal wall, such as a fibroma, neurofibroma or esophageal cyst. This statement undoubtedly was recorded by the X-ray Department after careful fluoroscopic study with barium, and must be accepted as final. Approximately a hundred benign tumors of the esophagus have been reported since 1717, and the diagnostic features have been fairly clearly defined. It is improbable that the x-ray staff of this hospital would have missed such a diagnosis.

Any mass of the superior mediastinum that moves with swallowing is probably a substernal goiter, on a purely statistical basis. Substernal goiters, unless they are examples of goiter in aberrant thyroid tissue, always have an attachment to the lower pole of the thyroid gland. In consequence, the tracheal deviation they cause begins

the thyroid cartilage and extends downward to the lower margin of the substernal extension, being maximal at the line of greatest tumor diameter. There is only an exception of 1 per cent to this rule. In the case under discussion, the tracheal deviation did not begin at the thyroid cartilage, but lower at the level of the first thoracic vertebra. Again, substernal goiters descend anteriorly to the trachea, but there is an exception of 1 per cent to this rule. However, 95 per cent of all goiters lying behind the trachea within the chest cause palpable and recognizable irregularity within the neck. Since the neck of this patient was normal, the combined statistical likelihood that she had a substernal goiter becomes 0.05 per cent, leaving it a possibility but not a probability. A so called "bronchiogenic cyst," arising from the right posterior margin of the trachea, could produce the symptoms and findings here recorded, and this is my diagnosis.

DR. EDWARD D. CHURCHILL. I might have been comforted if I had known these accurate statistical chances of the patient's having a substernal goiter, because, not knowing what the mass was, my chief worry was whether it could best be approached through the neck or through the chest. I did not want to operate through the chest and find a substernal goiter. It also crossed my mind that this might have been a parathyroid tumor arising in the posterior mediastinum. High lying posterior mediastinal tumors can in general be

delivered very readily through a cervical incision. I decided on the transthoracic approach and was correct, because this mass was intimately adherent to the lateral aspect of the trachea throughout its whole extent and could not have been exposed from above. It had to be separated from the trachea by sharp dissection, which in some areas exposed the mucous membrane of the trachea.

CLINICAL DIAGNOSIS

Mediastinal tumor (? neurofibroma).

DR. ADAMS'S DIAGNOSIS

Bronchiogenic cyst.

ANATOMICAL DIAGNOSIS

Bronchiogenic cyst, arising from trachea.

PATHOLOGICAL DISCUSSION

DR. MALLORY. I have the specimen here. It was cystic, filled with very thick, partially inspissated, mucoid material. In its walls, numerous plaques of cartilage could be easily felt. On microscopic examination, it is evident that it is lined with ciliated epithelium and that it contains numerous mucous glands, cartilaginous plaques and occasional bundles of smooth muscle, in other words, all the various structures that go to make up the trachea or bronchi. Therefore, it can be classed as a bronchiogenic or tracheal cyst, as Dr. Adams predicted.

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CESAREAN SECTION IN MASSACHUSETTS

THE five-year study of cesarean sections in Massachusetts, sponsored by the Massachusetts Department of Public Health and the Section of Obstetrics and Gynecology of the Massachusetts Medical Society and supervised by Dr. Robert L. DeNormandie, has been completed, and a summary of the results appears in this issue of the *Journal*. The compilation and analysis of even a limited amount of data on such a large series of cases is an arduous task, and Dr. DeNormandie and his associates deserve a large measure of credit for carrying it through to completion.

The report necessarily falls far short of being a thorough statistical study, but it furnishes considerable prima-facie evidence of abuse of this operation throughout the State. How extensive this abuse is, in view of the limited information available, must be a matter of speculation. The two most frequent indications given for primary section were contracted pelvis or disproportion and dystocia. There is no way of knowing precisely what was meant by "dystocia." The term simply means difficult childbirth. Presumably what was meant in most cases was so-called "cervical dystocia" or labor which, though prolonged, was ineffectual in dilating the cervix. These two indications combined account for 3234 cesarean sections, practically 1 per cent of the total births. It hardly seems plausible that in 1 out of every 100 cases of childbirth in Massachusetts, a section is necessary because the pelvis is too small, the baby too big or the labor ineffective. The third most frequent indication for primary section was placenta previa, of which there were 1021 cases. If all these patients had placenta previa, the incidence of that complication was about 1 in 327 births, and if there were any patients with placenta previa who were not delivered by cesarean section, the incidence was, of course, correspondingly greater. Such a frequency of placenta previa is scarcely credible. If the repeat sections are excluded, it appears that in 330,464 births there were 7763 primary sections—an incidence of about 1 in 43. The mere perusal of the indications given for some of these sections is sufficient to arouse suspicion. In 150 cases, they are, to judge by the samples given, utterly ridiculous, and in at least 170 others, they are manifestly indefensible.

The mortality in this series of cesarean sections is extraordinarily low—2.5 per cent. A low mortality, however, is not an unmixed blessing, because it is a contributory cause of the reckless use of the operation. With a mortality risk of this order of magnitude, it is not at all improbable that even a busy physician will practice many years without having a death follow cesa-

an section, and undoubtedly many a physician much more influenced by his personal experience than by a statistical fact. When the mortality of cesarean section is between 1 and 2 per cent, the operation is not more hazardous than are some of the more difficult and complicated pelvic deliveries, and if the operator in a difficult or complicated pelvic delivery is not especially trained in obstetrics, section is probably less hazardous. When, however, a healthy woman who could be delivered simply and easily through the pelvis is subjected to cesarean section, her chance of dying is multiplied about ten times. This is a truth that certainly is not widely known among the laity and seems not to be comprehended by many physicians.

The extensive use of cesarean section is not, of course, so great a factor in total maternal mortality as it is often said to be. A large proportion of all maternal deaths follow cesa-

rean section, but this is due, in part at least, to the fact that the operation is often employed to deliver patients with such serious complications as heart disease, nephritis, severe pre-eclampsia and placenta previa. These patients run a much greater risk than normal patients, regardless of how they are delivered. During the five years covered by this study, the total maternal mortality dropped from 4.1 to 2.9 per 1000 live births. The incidence of cesarean section, however, remained practically constant, and the slight drop in cesarean mortality is quite insufficient to account for the drop in total mortality. What is needed is not simply fewer cesarean sections, but better obstetrics, and the really disturbing feature of this report is not the number of sections done, nor the frequency of foolish indications, but the indirect evidence that there is still a great deal of bad obstetrics being done in Massachusetts.

OCCUPATIONAL SKIN DISEASE

WARTIME industrial activities have provided the Nation not only with a host of victims killed and permanently disabled by injury but also with much disability because of cutaneous damage. Not everyone is aware of the fact that 65 per cent of disease due to occupational factors concerns the skin, or that the consideration of occupational liability may arise in a fifth of all cases with cutaneous involvement, especially if the hands and arms alone are affected. Furthermore, the amount of disability produced by the effects of industrial processes on the skin has increased in the last few

months, owing, in all probability, to employees in new and unfamiliar occupations, perhaps inadequately trained in the cutaneous hazards involved and the proper care of the skin, to the speeding up of industrial processes, to the introduction of new ingredients and, perhaps, to other factors.

Particularly disturbing are the reports of increased irritation of the skin by cutting oils used in the manufacture of planes, tanks and guns. Numerous other examples of cutaneous hazards in war industries are cited by Downing elsewhere in this issue of the *Journal*.

For the medical profession, the early detection, the proper treatment and the prevention of occupational dermatoses constitute a real challenge. A review¹ of the recent report of the Committee on Industrial Dermatoses of the Section on Dermatology and Syphilology of the American Medical Association defines the criteria for the recognition of these diseases, and these points are further discussed in a recent issue of the *Journal*.² Proper treatment requires recognition of the causal factor and the development of proper protective measures or the elimination of that factor; and it implies the avoidance of presumably therapeutic

MASSACHUSETTS MEDICAL SERVICE

As of Tuesday, October 6, 1958
doctors had become participating
physicians in the Blue Shield.

substances that may exaggerate an already inflamed skin—20 to 25 per cent of all cases of dermatitis are due to some form of therapy. In prevention, however, lies the real answer. The working out of prophylactic measures against a particular cutaneous hazard is often difficult, but much progress has been made, as is indicated in Schwartz and Tulipan's³ recent textbook on the subject and in recent bulletins issued by the United States Public Health Service.

Occupational dermatoses are for the most part preventable. In these days, it is the duty of every physician to contribute to the war effort by recognizing these cases, by returning such patients to work at the earliest possible moment and by preventing further disability to them and other employees.

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2. Lane, C. G. Recognition of occupational dermatoses. *New Eng. J. Med.* 227:39-43, 1942.
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MEDICAL EPONYM

ROMBERG'S SIGN

Moritz Heinrich Romberg (1795-1873), professor and director of the Royal Polyclinic Institute of the Friedrich-Wilhelm University, Berlin, described this sign in his *Lehrbuch der Nerven-Krankheiten des Menschen (Textbook of Human Nervous Diseases)*, (Berlin, 1851: Vol. 2, p. 185). A portion of the translation follows:

If the patient is asked to close his eyes while standing upright, he immediately begins to sway and reel. . . . I called attention to this pathognomonic sign ten years ago (according to my observation, it does not occur either in other paralyzes or in uncomplicated blindness) and have since never failed to find it in any of my numerous patients with this disease.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE A PLEA FOR BREAST FEEDING

The war emergency has precipitated many changes in activities for the public good. Perhaps no more important contribution, particularly in view of the threatened shortage of physicians, can be made for this and the coming generation than by renewing the efforts to urge mothers to nurse their babies.

In their textbook, *Diseases of Infancy and Childhood*, Holt and McIntosh state:

Maternal nursing is the natural and ideal method of infant feeding. Every mother should nurse her infant unless there are weighty reasons to the contrary. The large majority can do so. The physician should do all in his power to encourage maternal nursing and to insure its success.

This statement of facts cannot be more succinctly expressed. The depleted ranks of the medical profession, the increase in the birth rate and the modified and often unfavorable conditions for infant care emphasize the importance of the above statement and the duty of the physician in this emergency.

Lactation can be promoted by the practice of the accepted principles of prenatal care, with emphasis on a well-balanced diet. And, of great importance in establishing lactation are skillful obstetric care and the proper education of nurses in the technic of breast feeding. Psychology plays no little role, especially in the early stages of lactation, and the nurse, by her skill and encouragement, is often the determining factor.

The technic of nursing consists in regularity of feedings, preferably every four hours on both breasts, five or six times daily. Complete emptying of the breast stimulates the secretion of milk, and a normal infant secures its quota of milk in twelve minutes of active nursing. Although the duration of each nursing cannot be empirically stated, it certainly is undesirable to urge babies to nurse beyond a twenty-minute period.

A common error is to omit nursing because the baby has not gained according to certain standards. A stationary weight or a slow gain for a week is often followed by an adequate supply of mother's milk. Furthermore, vomiting and loose stools are too often attributed to "poor milk." In general, a mother's milk is suitable for her infant, and these symptoms are only rarely of importance.

Since over 80 per cent of all babies in Massachusetts are born in hospitals, it is the responsibility of the nursing staffs and the visiting physicians to institute all the procedures that are necessary to ensure maternal nursing.

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DEATH

MIKOLAITIS — CASIMIR JOHN MIKOLAITIS, M.D., of Lawrence, died July 7. He was in his fifty-ninth year.

Dr. Mikolaitis received his degree from the Chicago College of Medicine and Surgery in 1914. He was a former member of the Massachusetts Medical Society.

WAR ACTIVITIES

OFFICE OF CIVILIAN DEFENSE

SUPPLEMENTAL STAFFS FOR EMERGENCY BASE HOSPITALS

Selected hospitals and medical schools in the coastal states have been invited by the Surgeon General of the United States Public Health Service to organize affiliated staff units that will be ready to serve when needed to supplement the medical staffs of emergency base hospitals, now being designated by the Medical Division of the Office of Civilian Defense. These units resemble the affiliated hospital units of the Army except that they are smaller. They are being organized to assure suitable status and remuneration for physicians who may be called on in the event of an enemy attack in their locality to care for casualties and other patients who have been evacuated to the interior of their region.

The designation of emergency base hospitals and the formation of affiliated units are part of a joint hospital program of the Medical Division of the Office of Civilian Defense and the United States Public Health Service. The program is authorized under an agreement concluded March 2, 1942, between the Federal Security Administrator and the director of the Office of Civilian Defense.

Physicians in the affiliated units will be commissioned in the inactive Reserve Corps of the Public Health Service. Unless an urgent need for their services should arise, they will remain on an inactive status for the duration of the war. They will be called to active service only if hospitals in their regions must be evacuated and the civilian population must be moved because of military necessity. Activation of the units will take place by order of the Surgeon General at the request of the chief medical officer of the Office of Civilian Defense on advice of

the regional medical officer and the state chief of Emergency Medical Service in charge of the affected areas.

The commission will be in grades ranging from passed assistant surgeon to senior surgeon, and when units are activated, these officers will have the rank, pay and allowances equivalent to those of officers in the armed forces.

Institutions invited to form units are asked to nominate an outstanding physician or surgeon as unit director, who, if he meets the physical and other requirements, will be commissioned senior surgeon in the Public Health Service Reserve. The unit director will then nominate the remainder of the staff, and appointments will be made after clearance through the state chief of Emergency Medical Service. Nominations are to be limited to male physicians over forty five years of age, to those under that age who have physical disabilities that disqualify them for military service but that do not interfere with their professional activities, and to women physicians.

To avoid serious depletion of the professional staffs in the medical schools and hospitals of the target areas, the Surgeon General has recommended that medical schools draw their affiliated units in part from associated hospitals and that nonteaching hospitals invite physicians from other qualified hospital staffs to collaborate.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST 1942

DISEASES	AUGUST 1942	AUGUST 1941	FIVE YEAR AVERAGE*
Anterior poliomyelitis	2	45	44
Chicken pox	121	125	106
Diphtheria	12	6	11
Dog bite	10/7	9/8	10/9
Dysentery bacillary	4	79	20
German measles	83	31	25
Conorrhea	49	283	401
Measles	296	281	287
Meningitis meningococcal	19	3	5
Meningitis other forms	2	4	5
Mumps	271	23	150
Paratyphoid infections	13	9	19
Pneumonia lobar	121	4	100
Scarlet fever	224	195	118
Syphilis	354	341	391
Tuberculosis pulmonary	303	270	297
Tuberculosis other forms	74	24	30
Typhoid fever	10	8	10
Undulant fever	6	13	4
Whooping cough	63	575	520

*Based on figures for preceding five years after bacillus meningitis only other form reportable previous to 1941

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Braintree, 1; Weymouth, 1, total, 2.

Diphtheria was reported from Athol, 1, Cambridge, 1, Fall River, 3, Lowell, 1, New Bedford, 1, Somerset, 1, Somerville, 1, Springfield, 1, Woburn, 2, total, 12.

Dysentery, bacillary, was reported from Boston, 1, Danvers, 1, Lowell, 1, Salem, 1, total, 4.

Encephalitis, infectious, was reported from Weston, 1, Weymouth, 1, total, 2.

Lymphocytic choriomeningitis was reported from Worcester, 1, total, 1.

Malaria was reported from Boston, 1, Camp Edwards, 3, Fort Banks, 1, Quincy, 1, total, 6.

Meningitis, meningococcal, was reported from Boston, 6, Brockton, 1, Cambridge, 2, Dedham, 1, Fort Devens, 1, Fitchburg, 2, Plymouth, 1, Revere, 2, South Hadley, 1, Springfield, 1, Worcester, 1, total, 19.

Meningitis, other forms, was reported from Natick, 1, Revere, 1, total, 2.

Paratyphoid infections were reported from Amherst, 4, Arlington, 1, Leominster, 1, Lowell, 1, Methuen, 1, Southwick, 1, Tyngham, 1, Woburn, 2, Worcester, 1, total, 13.

Septic sore throat was reported from Boston, 1, Lynn, 1, Milton, 1, Waltham, 1, Worcester, 1, total, 5.

Tetanus was reported from Holyoke, 1, total, 1.

Trachoma was reported from West Boylston, 1, Worcester, 1, total, 2.

Typhoid fever was reported from Arlington, 1, Beverly, 1, Cambridge, 2, Lynn, 1, Quincy, 1, Rockland, 1, Worcester, 3, total, 10.

Undulant fever was reported from Cambridge, 1, Clarksburg, 1, Fitchburg, 1, Townsend, 1, total, 4.

Communicable diseases reported at figures above their five-year averages were chicken pox, diphtheria, German measles, gonorrhea, measles, pneumonia, scarlet fever, pulmonary tuberculosis, whooping cough and mumps. The last disease had been previously reported at record high figures for eleven of the preceding twelve months.

Meningococcal meningitis was reported at a record high figure.

Anterior poliomyelitis reached a record low figure during this month.

Diseases reported at lower figures than their five-year averages include dog bite, bacillary dysentery, paratyphoid infections, syphilis and tuberculosis, other forms.

Typhoid and undulant fevers were both reported at figures equal to their five-year averages.

Two cases of animal rabies were reported, one from each of the foci in the southeastern and northeastern sections of the State.

CORRESPONDENCE

APPROVED LABORATORIES FOR PREMARITAL BLOOD TESTS

To the Editor: The list of laboratories approved for performing premarital blood tests has recently been revised. There are eight such laboratories on the present list in addition to the Wassermann Laboratory of the department. These are:

Boston

Boston Dispensary
Boston Health Department
Leary Laboratory
Massachusetts General Hospital
Peter Bent Brigham Hospital

Brockton

Health Department

New Bedford

St. Luke's Hospital

Springfield

Mercy Hospital

Several other laboratories have made application for approval. It is likely that others will be added to the list about January 1.

PAUL J. JAKUBOWICZ, M.D.
Commissioner of Public Health

State House
Boston

Cholesterol is synthesized in the human body. The excess is probably ingested in the form of egg yolk, milk and animal fats. Needs for this substance are greatest in times of rapid cell formation. Egg yolk is intended for the embryo, and milk for the nursing. Metabolism of cholesterol is most efficient in the young, but heredity is certainly a factor. The tissue content of cholesterol increases with age, whereas the need for it grows less. Women mobilize this substance during pregnancy, possibly for the use of the embryo, and show minor mobilization during menstruation. They are less susceptible to atherosclerosis than men.

Excess cholesterol, then, is the cause of atherosclerosis, but stresses determine the localization of the lesions. Sex and thyroid secretions influence cholesterol metabolism, and age and heredity are modifying factors. Diets with limited or absent cholesterol should prevent atherosclerosis, and this may be accomplished by the substitution of vegetable oils, whose sterols are not absorbed, for animal fats.

The lesions of coronary sclerosis are almost exclusively atherosclerotic. The frequency of coronary disease is related to the unusual stresses to which the vessels are subjected. These vessels arise directly from the aorta in a region where there is maximal stress when the aortic cusps close. Moreover, circulation is cut off from the muscular branches by compression as the ventricles contract. At the same time, the main vessels and their sub-epicardial branches are not compressed, but are filled with blood under systolic pressure, without being able to empty themselves. The main coronary circulation is during diastole. Because of these stresses, normal coronary arteries develop characteristic thickening of the intima to produce a "buffer layer."

Advanced coronary sclerosis in patients as young as twelve years indicates that atherosclerosis is not entirely a disease of old age. But the type of lesion varies with age. In youth, excess cholesterol provokes a growth of loosely textured fibroblastic tissue. As the lesions enlarge, diffusion of nutritive material from the circulating blood becomes inadequate, and necrosis of the deep layers results. When the lesions become even larger, vascularization by capillaries from the lumen, or less commonly from the vasa vasorum, supplies the nutriment. All advanced coronary lesions are vascularized. The lumen is narrowed by eccentric or concentric thickening of the intima. Spasm may result in rupture of capillaries, fibrin formation and fibrinoid necrosis. With extension of the necrosis to the endothelium, thrombosis follows, and is the usual cause of sudden death.

In middle age, more collagen is formed, and scarring is typical of this period. Narrowing of the lumen, with coronary insufficiency and chronic vascular myocarditis, is frequently found at post-mortem examination. Spasm may result in sudden death or in infarction without anatomic occlusion of the vessels, particularly in hypertensive heart disease. Thrombosis is less common than in youth, whereas calcification becomes commoner.

In old age, atherocheumas occur frequently because of lowered tissue reaction to excess cholesterol. Occlusion may be caused by rupture of such a lesion. Scarring persists from earlier periods, and calcification is practically the rule.

Rupture through the necrotic tissues of a cardiac infarct may cause death by hemopericardium and cardiac tamponade. Rupture of an atherosclerotic coronary artery may likewise lead to hemopericardium. Dissecting aneurysms of the coronary arteries are rare. Infarcts are re-

paired by granulation, sometimes with pericardial adhesions. Mural cardiac thrombi may lead to systemic embolism. The scar tissue repairing an infarct may undergo stretching, producing a cardiac aneurysm. Coronary thrombi undergo organization if the patient lives, sometimes with canalization. But, usually, the blood flow is re-established around the region of thrombosis by a collateral circulation. Anastomoses between coronary arteries increase with age. In conclusion, it was pointed out that coronary occlusion may be symptomless, or may cause mild or serious illness; it may result in sudden death with ventricular fibrillation or death so instant as to suggest immediate cerebral arrest with cardiac and respiratory standstill.

The discussion was opened by Dr. Alan Moritz, who questioned the existence of coronary spasm. But Dr. Leary replied that coronary infarcts without thrombosis can be demonstrated at autopsy and that death sometimes follows characteristic manifestations of coronary occlusion when minor post-mortem lesions are present, if any. Dr. Samuel Levine pointed out that in a study of 100 young patients with angina pectoris, 96 were males. He added that this indicates a strong endocrine factor; however, the localization of the atheromatous lesion seems to be a familial factor, possibly dependent on some congenital anatomic peculiarity. Dr. Leary suggested that the prevalence of the proximal portion of the left coronary artery as a site for a single thrombosis may be explained on the basis of the sharp angulation of this vessel and its main branch, which create a mechanical hazard in a person who is unable to handle cholesterol adequately.

In answer to questions from the floor, Dr. Leary stated that the blood cholesterol levels in experimental rabbits, as well as in patients with hypothyroidism, are elevated. At autopsy, the amount of atherosclerosis is roughly proportional to the amount of hypothyroidism, whereas hyperthyroid patients definitely have less or no atherosclerosis. The changes described in the liver and adrenal glands in the rabbit have not been observed in man. The relatively enormous accumulations of excess cholesterol in these organs in the experimental rabbit, whose normal diet includes no cholesterol, account for this difference. Lesions due to intermittent accretions of excess cholesterol over a period of years in man may be reproduced in weeks or months in the rabbit.

BOOK REVIEW

Neuroanatomy. By Fred A. Mettler, M.D., Ph.D. 4th ed., cloth, 476 pp., with 337 illustrations, including 30 in color. St. Louis: The C. V. Mosby Company, 1942. \$7.50.

This is a new and valuable addition to the textbooks of neuroanatomy. The first part deals with the gross aspects of the neural systems, and the second, with microscopic anatomy. The text is clear, concise and simple in terminology. The illustrations, some in color, are a particular feature of the book. The drawings are excellent and the labeling adequate, and the figures are well correlated with the text. Adequate references to the literature are given, and the index is generous.

The author is to be congratulated on the quality of his product. In a field already covered by many other books, he has succeeded in writing a text that is superior to most. The format and press work are well fitted to the text. The book is worthy of the highest endorsement.

(Notices on page x)

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SYMPOSIUM: MINOR PSYCHIATRIC DISTURBANCES IN WAR AND CIVILIAN LIFE

THE DIAGNOSIS OF THE PSYCHONEUROSES

DONALD J. MACPHERSON, MD †

BOSTON

IN a discussion of the phenomena included in the term "psychoneuroses," it is essential to realize that the word does not apply to a specific disease but rather to the quality and degree of adjustment that a person makes to the problem of living. It relates to his satisfaction with life, the efficiency with which his abilities are mobilized and his effect on other people.

Although in certain cases there may be a constitutional predisposition to behave in a neurotic manner, it appears equally true that under fatigue, sufficient stress or a particular kind of stress, a normal person may for a time behave in a neurotic manner.

Before the actual experience with bombing in Britain, there was apprehension that civilians exposed to the intense and terrifying conditions created by air raids would react with panic, hysteria or neurosis. As a matter of fact, this has not happened. Under this kind of stress, pride or the fear of what other people might think is sufficient to maintain a freedom from neurotic manifestations. People become habituated to the threat of destruction very quickly and go about their affairs. There may be anger at the enemy, but that might well be classified as righteous indignation. Pathologic mental disturbance is extremely rare. Among people known to be neurotic, about 25 per cent have actually improved under war strain. This may be because the demands and opportunities for activity under the altered conditions are more vital than the issues creating the neuroses. Twenty-five per cent are made worse, and 50 per cent show little or no change. Children appear to be even

less disturbed by air raids than adults. In general, there is a tendency for them to imitate adult behavior. It is interesting that the disorganization of a regular routine of life is more frequently a cause of neurotic behavior than the air raids per se.

In normal civilian life, some patients who seek help and are recognized as neurotic may be in trouble either because of a temporary conflict brought on by unusual environmental or personal difficulty that will pass or change with time, or because of a type of personality that has difficulty in adjusting to a normal environment most of the time. In the latter group, certain tendencies, which constitute a variation from what might be considered mature adult behavior, appear very often. A healthy-minded adult has acquired a capacity to observe his environment and appraise himself with some objectivity. With these data, action is initiated with respect for real limitations and without excessive optimism or pessimism about the results. He does the best he can and is willing to make mistakes and learn from them.

The neurotic has a strong subjective bias. He has intense wishes and fears. His behavior tends to be governed by attempts to protect his own feelings. He is prone to disregard facts that are inconsistent with his wishes, and to have difficulty in learning from experience. He may be puzzled, angry or hurt at the ineffectiveness of his efforts, but he continues to make the same mistakes. There is a strong tendency to assume that the trouble is with other people, or bad luck. One is reminded of the poor workman who blames his failure on the tools.

The neurotic does not consider himself realistically, as an object in a world of objects subject to natural law. He feels special, and eternally hopes

†This and the two subsequent papers were presented at the annual meeting of the Massachusetts Medical Society, Boston, May 27, 1942.

Instructor in medicine, Harvard Medical School; consultant, Peter Bent Brigham Hospital.

PSYCHIATRIC COMPONENTS IN MEDICAL DISEASE: PSYCHOSOMATIC MEDICINE*

JACOB E. FINESINGER, M.D.†

BOSTON

DURING the last two decades, a new field has opened for the investigation of certain medical illnesses in which psychiatrists have shown interest. This field, often referred to as psychosomatic medicine, deals primarily with medical and surgical diseases that are properly within the province of internists, surgeons and medical specialists. The illnesses studied are those in which there exists a pathologic lesion, in contrast to the psychoneuroses, — especially hypochondriasis, — in which no known pathology exists. The etiology of these illnesses is as a rule unknown. Repeated observations have demonstrated that stresses and strains arising from the environmental situation and from difficulties in the personality of the patient play a significant role in the precipitation and in exacerbations of these illnesses. From studies in the neuroses and psychoses, psychiatrists have become familiar with the significance to the patient of specific situations and with the intricacies of personality function. This information has been applied to psychosomatic medicine in the hope of throwing light on the puzzles presented to the physician by these illnesses. The systematic approach to these special problems is still in its preliminary stage, and not more than the surface has been scratched. Yet sufficient work has already been done to indicate the validity of this approach. This paper reviews briefly the most striking studies that have appeared in this field.

It has been found that certain organ systems seem to be more readily involved than others. These systems are essentially those whose activities are actuated by the autonomic nervous system. One is apparently dealing with episodic reactions, which in many cases result in irreversible pathologic processes. The typical feature of these illnesses is that they are of long duration and characterized by exacerbations and remissions; they strongly resist treatment. Certain factors, especially allergic factors, play a role in the development of some of these disorders and yet do not alone explain the exacerbations and remissions. Of the many and confusing interrelations presented by the study of these illnesses, the best established seems to be a temporal relation between exacerba-

tions and events or situations confronting the patient. In a few illnesses, a relation between the clinical diagnosis and the personality of the patient seems established from several sources. The role that situations and personality factors play in the etiology of the illness is least well established.

Studies that have been undertaken have made use of three methods of approach. Most of the studies concerned with establishing correlations depend on the history obtained from the patient or from some other source, by means of interviews or questionnaires. Even though large numbers of patients can be studied in this way, the limitations and sources of error are obvious. One would have to have access to data dealing with every single exacerbation and remission of the illness, a task hardly possible by the history method. The dependence on the memory of the patient and the avoidance of suggestion on the part of the interviewer represent the major difficulties. In dealing with the personality traits of patients, one is faced by the added difficulty of using descriptive words, about which there is little agreement among investigators.

Another approach concerns itself with the careful and intensive study of small groups of patients, either by intensive psychiatric study or by rigid psychoanalytic procedure. Here, too, correlations are drawn between situations and the exacerbation or remission of symptoms. In addition, attempts have been made to modify the patients by means of various psychotherapeutic approaches so that the same persons would no longer react pathologically to the presenting stimuli. There are also therapeutic reports and a few follow-up studies in some illnesses.

A third and most significant approach has been used in a very few studies. This is the experimental approach, which in these problems attempts first of all to find out what specific situations or ideas correlate with the symptoms. Attempts are then made to bring about exacerbations by carefully introducing discussions about these situations or ideas into the interview during a state of remission, avoiding as much as possible the introduction of other complicating variables.

The illnesses in which information is moderately complete are presented in some detail. The others are briefly mentioned. No attempt is made to

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 27, 1942.

From the Department of Diseases of the Nervous System, Harvard Medical School, and the Psychiatric Department, Massachusetts General Hospital.

†Assistant professor of psychiatry, Harvard Medical School; psychiatrist, Massachusetts General Hospital.

include all the known facts. The literature has been comprehensively reviewed by Dunbar.¹

CLINICAL STUDIES

Gastrointestinal Diseases

That patients react with their gastrointestinal symptoms to various types of situational and emotional stimuli has long been known.² Cannon³ has clearly pointed out that states of worry and anxiety, grief, anger and other violent emotions can start a vicious circle leading through impaired digestion to mild inflammation and to impaired absorption, resulting in the vicious circle of emotional disturbances. Studies on patients with gastric ulcer, duodenal ulcer, esophageal spasm⁴ and gastrospasm⁵ have appeared in which the role of emotional factors has been considered. Recently, Mittelman, Wolff and Scharf,⁶ in a study of patients with gastritis, duodenitis and peptic ulcer, note that epigastric distress, nausea and even bleeding are precipitated or increased by emotional states. Anxiety, whether recognized by the patient or not, is an outstanding component of these emotional disturbances. In experimental work on patients with peptic ulcer, these authors report that such feelings as embarrassment, resentment, anger, anxiety and anxious anticipation are associated with a rise in gastric acidity and in total volume of secretion, with high or continuous peristaltic activity and hyperemia of the gastric mucosa. Feelings of security and relaxation are associated with low acidity and with less peristaltic activity. They postulate that the increased acidity, motility, hyperemia and even hemorrhage may have a bearing on the genesis of gastric and duodenal lesions found in the clinical picture of gastritis and duodenitis. The fact that mucosal erosions result from prolonged stimulation of the vagus⁷ and also follow the intravenous⁸ and intraventricular injection of acetyl-choline indicates that the parasympathetic outflow is most probably involved in the production of these lesions. It is not yet clear what factors determine the irreversible pathology that occurs in some cases.⁹

Psychosomatic studies on mucous colitis (mucous diarrhea), constipation, spasm of the colon and ulcerative colitis have been reported. Most of the work deals with mucous colitis, which was first well described by DaCosta.¹⁰ Later authors emphasized the secretory and motor changes,¹¹ the inflammatory basis of the illness¹² and the role of food allergy.¹³ White, Cobb and Jones,¹⁴ in a broad study of mucous colitis, support the thesis that this disease is a physiologic disorder of the colon brought about by the action of the parasympathetic nervous system. The pathologic changes

seen can be brought about experimentally by the use of cholinergic drugs,¹⁵ although these changes have not been produced by the stimulation of the sacral outflow of the parasympathetic nervous system. In 92 per cent of the 56 psychogenic cases studied by White, Cobb and Jones, emotional tension was present, and the authors believe that this emotional tension was the commonest cause of the parasympathetic stimulation. In the more neurotic group of their patients, exacerbations of symptoms were associated with emotional tension in 56 per cent, whereas in the less neurotic group, a relation between tension and exacerbations of symptoms was found in 85 per cent. The higher correlation obtained for the less neurotic group was believed due to the fact that the emotional disturbances in this group were more frequently recognized, since "the sources of tension were always superficial and more readily understandable."

From a psychoanalytic study of a small number of patients, Alexander¹⁶ reported three personality types associated with gastrointestinal symptoms. He considered that patients with primarily gastric symptoms had personality features characterized by activity, independence and efficiency. Of the patients with intestinal complaints, he distinguished a "colon type" with diarrhea as dependent persons who had marked tendencies toward giving, with feelings of obligation and guilt. He also differentiated a "constipation type," characterized by stinginess, dependence and need for accepting with no guilt and no need for giving. White, Cobb and Jones¹⁴ confirmed the existence of these types among their patients. They were unable to corroborate fully the correlation postulated by Alexander between the colon and constipation types and the presence of constipation or diarrhea. White, Cobb and Jones found that the emotion most characteristic of their patients was that of resentment. Patients with mucous colitis were also conscientious, rigid, meticulous people with compulsive tendencies. As a result of this rigidity of thinking and the tendency to dwell on disturbing topics, the tension was sustained over long periods. This protracted state of affairs is believed to result in the formation of symptoms.

In patients with ulcerative colitis, correlations between the exacerbations and special situations have been reported by Murray,¹⁷ Sullivan¹⁸ and Wittkower.¹⁹ Lindemann²⁰ has most recently pointed out that these patients present a psychiatric disturbance characterized by apathy, a marked difficulty in communicating matters of emotional concern and a defect in "differentiating reality from subjective falsifications." Daniels²¹ has em-

phasized in this group the need for dependence on some member of the family, usually the mother. Conflict develops in situations, such as engagement and marriage, that threaten this dependence. This conflict can be the precipitating factor.

Allergic Diseases

Investigations have been made on various diseases associated with specific allergens. Of these, the most work has been done on asthma²² and on certain types of cutaneous disturbances, notably atopic dermatitis.²³ That the respiratory function can be influenced by emotions and situations has long been known. More recently, this question has been re-investigated, and it has been shown that, in anxiety states and hysteria, changes in rate of respiration, in total ventilation and in the pattern of respiration are associated with certain ideational and sensory stimuli.²⁴ Irregularities in respiratory rhythm are described in anxiety states,²⁵ and marked episodes of hyperventilation have been seen in hysteria.²⁶ These changes are all episodic and reversible.

Bronchial asthma. Many sporadic studies show that in acute attacks of asthma not only exacerbations of the condition but also, at times, remissions are associated with situations that provoke acute anger²⁷ or other violent affects. The demonstration of sensitivity on the part of patients to many allergens not only has removed the emphasis from the emotional factors for a time but also has made it difficult to exclude the possibility that every asthmatic attack is caused by an allergen unsuspected in the situation. Yet, in many cases, the presence of allergens to which the patient is sensitive does not alone explain the attack. Such factors as fatigue and emotional disturbances have been secondarily involved. More recently, evidence has been accumulating that asthmatic attacks can be brought on by hypnosis in asthmatic patients,²⁸ and even by direct suggestion²⁹; the fact that several authors have used psychotherapy with good results when somatic therapy failed³⁰ has reopened the problem for systematic investigation.

McDermott and Cobb³¹ found that in a two-hour interview an emotional component could be found in 37 out of 50 consecutive cases of asthma admitted to the Massachusetts General Hospital. The same finding was mentioned by Halliday³² in a series of 30 patients. French and Alexander³³ have recently reported a study of 27 patients with bronchial asthma who were psychoanalyzed at the Chicago Institute of Psychoanalysis. Nineteen of these patients were under treatment for long periods, and the results have been reported in detail. The thesis advanced by this group of investigators is that asthmatic patients tend to respond

to increased respiratory stimulation with asthmatic attacks. Hence, attacks follow situations or experiences that induce respiratory stimulation, such as intense emotion, muscular exertion and hurry. They also note the paradoxical observation that, in some cases, intense emotion has been known to bring about the cessation of an attack. As a tentative explanation of the paradox, French and Alexander suggest that the precipitating situations are those in which the patient "must suppress his emotion or in which he finds himself completely helpless to give adequate expression to it." They refer to the observation of other authors³¹ that in cases in which the attack ceases on sudden emotion, adrenalin is mobilized in the blood stream; this mechanism apparently does not operate during the emotional conflict induced by the precipitating situation. From their analytic material, they find that the conflict situation relates to earlier situations that threaten to separate the patient from a female figure—a mother figure. The patient responds to this state of helplessness by an asthmatic attack, which according to these authors has the symbolic significance of a suppressed cry.

Deutsch³⁴ has postulated that the asthmatic patient undergoes a development characterized by an "affection" of the respiratory apparatus in early childhood associated with certain emotional factors at that time, emotional upsets in childhood, acting as conditioning factors, and the development of a marked dependence on a hated, domineering and aggressive mother.

Rogerson, Hardcastle and Duguid³⁵ report that practically all their asthmatic children were characterized by marked anxiety and lack of self-confidence. In the adult group, French and Alexander³³ found that their patients all suffered from a deep-seated insecurity and a more or less intense need for parental love and protection.

Atopic dermatitis. Atopic dermatitis is another chronic illness in which there are marked exacerbations and remissions. Most of the patients with this disturbance show sensitivity to specific allergens, and many have personal or familial histories of other allergic disturbances. Becker³⁶ has repeatedly pointed out that fatigue may play a major role in the etiology through its effect on the underlying "protoplasmic irritability," which, according to him, is constitutional. Stokes³⁷ has emphasized the relation between skin disturbances and psychosexual difficulties. Other workers have pointed out the significance of blushing,³⁸ exhibitionism³⁹ and the need for self-punishment.⁴⁰

Greenhill and Finesinger⁴¹ have found that situations dealing with work problems, family difficulties, psychosexual problems and changes in the

physical environment were associated with the exacerbation of symptoms. In this respect, the results confirm earlier studies of Becker and Obermayer.⁴³ These events were associated primarily with feelings of hostility, insecurity and depression. On the other hand, a smaller series of patients with lupus erythematosus discoides also showed a relation between situations and exacerbation of symptoms. This correlation was not nearly so striking as that in the atopic patients. The patients with atopic dermatitis had the characteristics of the compulsive obsessive type, as well as difficulty in their relations with other people. There was a great incidence of feelings of hostility rarely shown in overt action. These patients were sensitive and tended to suppress feelings of anger. They entertained feelings of inadequacy, lacked self-confidence and were depressed and notably shy.

Other diseases. Certain studies have been concerned with urticaria,⁴² angioneurotic edema,⁴³ hay fever⁴² and the common cold.⁴⁴ Saul and Bernstein⁴² believe that states of repressed, intense, frustrated longing are of primary importance complementing allergic factors. They also mention the interesting fact that urticaria appeared in 1 case when weeping was repressed and often terminated when the patient wept. Saul⁴² has more recently confirmed the role of repressed longing in cases of hay fever and common cold.

Cardiovascular Diseases

Some of the earliest observations deal with the effects of situations and emotions on the cardiovascular system.⁴⁵ Acute cardiac and cerebral insults have been repeatedly described following emotional outbursts. In some cases, excitement and anger apparently bring about a rise in blood pressure, which causes breaks in peripheral vessels already weakened by an existing lesion. Likewise, acute transitory changes in blood pressure,⁴⁶ pulse rate⁴⁷ and cardiac output⁴⁸ are known to be associated with disturbing situations and with various emotions. Similar episodes are known to produce exacerbations in other illnesses, such as Raynaud's disease⁴⁹ and essential hypertension,⁵⁰ in which a vascular lesion already exists. Distinct personality trends have been described by Hamilton⁵¹ in patients with elevated blood pressures.

The more detailed studies are concerned with essential hypertension. It has been suggested that essential hypertension is associated with unstable and tense personalities. The behavior of such persons is characterized by increased psychomotor activity.⁵²⁻⁵³ Alexander⁵⁴ and Saul⁵⁵ have studied several patients psychoanalytically in whom a diagnosis of essential hypertension was made. They state that the basic problems in these patients are

concerned with attempts at handling their dependence. This dependence has its origin in an early relationship to a dominating parent, and leads to the formation of a pattern of general behavior to which the patient adheres thereafter. It is this submission to authority that the patient struggles against with rebellion and hostility. The conflict centers about the expression or repression of this hostility. During periods when either the dependence or the hostility could be gratified, the blood pressure was markedly lower. This formulation has been confirmed by Miller⁵⁶ in a study of psychotic patients with high blood pressure.

Endocrine Disturbances

Numerous studies in the literature deal with the relation between various endocrine disturbances and the psychoses.⁵⁷⁻⁵⁸ The effects of adrenalin on psychoneurotic patients, especially in anxiety states, has been investigated.⁵⁹ This whole field has been reactivated by the development of new and accurate methods of measuring estrogens, androgens, gonadotropin and pregnenediol, and by the more current study of vaginal smears. Correlations have been drawn between various phases of the menstrual cycle and instinctual drives, types of phantasies and dream productions.⁶⁰ The relation between androgens, estrogenic substances and the clinical picture is reported in studies on homosexuality⁶¹⁻⁶² and hermaphroditism.⁶³

Of the various medical illnesses associated with endocrine disturbances, the most work has been done on hyperthyroidism (Graves's disease). As a result of studies in several large series of cases,⁶⁴⁻⁶⁶ it has been established that emotions associated with sudden fright or other psychic trauma frequently precede the onset of the illness. The appearance of exophthalmos and enlargement of the thyroid gland can appear within a few hours after the fright. Yet, according to Rahm,⁶⁶ these acute situations play a less important role in the precipitation of symptoms than do chronic worries or continuous anxiety. Little work has been done on the personality of patients with hyperthyroidism.⁶⁷

Rheumatoid Arthritis

In rheumatoid arthritis, one is dealing with a disease of unknown etiology characterized by exacerbations and remissions. Although the factors playing a role in the onset of the disease and its exacerbations are unknown, some authors have suggested that emotional disturbances, anxiety and worry play a significant role.⁶⁸ Cobb, Bauer and Whiting⁶⁹ found that in a series of 50 patients with typical rheumatoid arthritis, a significant relation between disturbing situations and the arthritis occurred in 60 per cent. The situations

found alone or in combination included financial distress, family difficulties, the loss of a parent or spouse and unfaithfulness of a married partner. The effect involved was usually that of worry. Further studies on the personality of these patients are still in progress.

Epilepsy

Among a long list of the factors that play a role in producing convulsions, Cobb⁷⁰ has listed emotional shock as one that is effective in producing vasoconstriction. He mentions that fright, anger and other strong emotions may cause pallor of the face and changes in circulation elsewhere in the body. In a study on 36 patients, Fremont-Smith⁷¹ found a direct relation between emotional tension and one or more of the major convulsions in two thirds of the cases. In several of the patients, all or nearly all the attacks had been immediately preceded by a strong emotion, usually that of fear, anger or frustration. Fremont-Smith was able to precipitate major or minor attacks in 8 of his patients by a discussion of the emotional difficulties. He concludes that, in many cases, the emotional tension acts as a precipitating factor for convulsive seizures, even though the patient may be unaware of this relation. Further studies on the unconscious mechanisms associated with fits have been reported by Kardiner.⁷²

Miscellaneous Diseases

The above summary deals briefly with some of the more complete studies in psychosomatic medicine. The literature contains reports dealing with many other varied conditions, such as anorexia nervosa,⁷³ glaucoma,⁷⁴ sciatica,⁷⁵ diabetes,⁷⁶ heart disease⁷⁷ and even fractures.⁷⁸ The development of greater interest in these problems has brought with it an ever-increasing number of observations in medicine and its specialties.

THE THERAPY

Therapy in psychosomatic medicine is similar to that used in the treatment of the psychoneuroses. The symptom can be considered a reaction of the patient to a stimulus, which may be simple or complex, and may be known or unknown to him. Psychiatric therapy attempts to modify the stimulus or the person reacting to the stimulus, or both. In many cases, modification or removal of the stimulus—that is, changing of the situation or removal of the patient from the situation—has been of therapeutic value. Other psychotherapeutic efforts have been directed toward changing the patient to enable him to withstand any situation without the need for pathologic reactions. Two methods are employed for this purpose. The first

makes use of reassurance, suggestion, persuasion and even hypnosis, and as such is very closely bound up with the relation between the physician and the patient. The success or failure of this procedure goes hand in hand with the vicissitudes of the doctor-patient relation. The patient acquires no understanding of the factors involved, and his improvement remains associated with the magic power of the physician. The second means of change depends on the acquisition of insight and understanding on the part of the patient into the factors associated with the onset and exacerbation of the symptoms. This is accomplished by the use of either distributive analysis or psychoanalysis. In the former, the physician makes use of discussion that is based on the patient's modes of reaction and on his methods of handling difficult situations, especially those that seem to have a direct relation to the complaint. In psychoanalysis, emphasis is placed primarily on the uncovering and understanding of earlier modes of reaction, unknown to the patient. Therapeutic successes have been claimed by the proponents of all the therapeutic methods mentioned. As yet, no single approach has completely won the field. This fact alone suggests that considerably more effort must be expended in the future before a universally accepted therapy is developed.

SUMMARY

Psychosomatic medicine deals with medical disturbances in which situational and emotional factors play a role in either the precipitation or the exacerbation of symptoms. The situations are, as a rule, associated with the unpleasant feelings of fear, anxiety, guilt, resentment, frustration and longing. These illnesses are found in persons who have conflicts in reference to the expression of hostility and anger; most of them do not have the frank symptoms of the psychoneuroses. Many studies indicate that these are people with obsessive tendencies who tend to ruminate over their difficulties and find it impossible to resolve them on account of indecisions. It may be that these tendencies present constant stimuli to the autonomic nervous system and eventually lead to chronic irreversible reactions in the end organs, resulting in a pathologic process. The fact remains that therapy has lagged far behind the understanding of these problems. Yet, at the present stage of information, the only practical approach in many illnesses appears to be that of psychiatric therapy. This is especially true in situations in which medical therapy as such has failed or is still lacking. The inadequacy of psychotherapy in many cases is a challenge toward improving

present methods or toward developing new methods. The value of psychotherapy, promising as it seems at present, can be established only through carefully controlled studies. This is the task of the future.

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THERAPEUTIC PROCEDURES IN PSYCHONEUROSIS*

ERICH LINDEMANN, M.D.†

BOSTON

PROCEDURES in the treatment of psychoneurotic conditions have not reached the simple level of known indications and expected results that has been attained in chemotherapy. Knowledge in the treatment of disease usually takes great strides forward when the disease can be reproduced in laboratory animals. Pavlov¹ was able to reproduce in dogs psychologic conflicts that made them behave like persons suffering from neuroses. He demonstrated pathologic nervousness and sleepiness. Liddell et al.² have similarly produced enduring derangements of behavior in sheep by a combination of stimuli and have treated them successfully with bromide medication. Some of their sheep developed a cardiac disorder shown by a rapid and irregular pulse brought on by stimuli that had no effect on normal animals. The animals were "conditioned," that is, taught to make discriminations between stimuli. When this process of discrimination is refined,—when it is made difficult by delay or interruptions,—neurotic behavior develops.

Maier^{3, 4} and Cook⁵ have carried out similar work with rats, and at a recent meeting of the American Psychiatric Association, Massermann⁶ presented evidence of neurotic behavior in cats that was produced by exposure to psychic trauma, which consisted in an annoying blast of air when, after having completed a task and opened a feedbox after a warning light had flashed, they were enjoying their reward and the satisfaction of their desire for food. He tried, and found successful, four different means of therapy: retraining by petting and reassurance, reinforcing and making inescap-

able the conflict situation, increasing the desire and strengthening the stimulus.

In human beings, the experimental production of neurosis and subsequent therapy have, for obvious reasons, not advanced so far, but laboratory research is stressed in clinics such as the Department of Psychiatry of the Massachusetts General Hospital.

A good many experiments were carried out years ago with hypnosis, by which it is possible to produce paralysis, anesthesia and changes in the skin capillaries and even minor changes in visceral functions (Charcot⁷ and Bernheim⁸). In addition, there are observations about events and their effect on the incidence of neuroses. The number of neurotic conditions during World War I increased vastly, whereas the number of schizophrenias remained the same, and the observations that are already being collected about the present war again throw interesting light on the effect of certain types of experiences on subsequent behavior. Mira,⁹ for example, mentioned first—and it was later restated by Miller,¹⁰ Gillespie¹¹ and Ross¹²—that the neuroses that might be expected to develop under the intense experiences of total war do not appear if the person has no possibility of securing refuge in a safe area but must instead remain in the situation. Furthermore, it has been found that separation of children from their families is much more effective in producing psychoneurotic disturbances than the experience of actual bombing.

None of these observations have up to now been systematic enough to suggest reliable systems of therapeutic procedures, and different psychiatrists still vary in their indications and choices of method. The powerful influx of a great deal of psychologic theory, which came about through the psycho-

*Presented at the annual meeting of the Massachusetts Medical Society Boston, May 27, 1942.

From the Department of Diseases of the Nervous System, Harvard Medical School, and the Department of Psychiatry, Massachusetts General Hospital.

†Associate in psychiatry, Harvard Medical School, associate psychiatrist, Massachusetts General Hospital.

analytic school and the psychobiologic school, has led to a whole new jargon that has served only to alienate the medical man from the whole work of psychiatric treatment. He has been content to develop his own trial-and-error procedures or to refer to a psychiatrist all the problems that made him feel uncomfortable, stopping his interest in the patient at that point. Psychotherapy was, however, first practiced by medical men, and one of the greatest contributors to the understanding of hysteria, Charcot,⁷ made all his demonstrations in the medical clinic.

In this presentation, an attempt is made to present very simply the methods used in the Out Patient Department of the Massachusetts General Hospital, the indications under which they are applied, and the success obtained with them.

DIAGNOSIS

Diagnosis necessarily precedes a decision regarding therapeutic approach. At present, the neuroses are classified as reactive depression, anxiety neurosis, hysteria, obsessive neurosis and hypochondriasis. It will be noted that neurasthenia is not mentioned; this condition, often labeled neurocirculatory asthenia, has in many cases been found to be either a mild depression or a mild anxiety state, or an infectious or hormonal disease. The other conditions may be briefly described as follows:

Reactive depression. The patient does not necessarily cry. The outstanding symptoms are slowness, inability to concentrate, hopelessness and, often, bewilderment. Medical disorders that the patient may have at this time—for example, asthma and gastrointestinal disturbances—may be aggravated. Some practice is necessary to recognize this condition because the patient often succeeds in his effort to hide his distress.

Anxiety neurosis. The picture is one of acute attacks with marked visceral disturbances (heart action, respiration and gastrointestinal function) and an intense subjective distress referred to as fear or nervousness. The free interval between attacks may be one of exhaustion.

Hysteria. This term is perhaps the most abused in the nomenclature of the neuroses, any dramatic behavior being described as hysterical. Among psychiatrists, it means rather a condition in which one finds paralysis, weakness, aphonia, vomiting and bladder disturbance without a discoverable lesion. It is usually accompanied by a striking absence of anxiety, even though the patient, on study, is found to live in a distressing situation. These pseudoneurologic symptoms characterize a large group of war neuroses, but under peacetime conditions they are seen chiefly in women.¹³

Obsessive neurosis. This is usually well understood: preoccupation with foolish thoughts or the necessity of carrying out absurd or childish actions disturbs the patient.

Hypochondriasis. An important distinction must be made between anxiety neurosis, with evidence of genuine disturbance in the circulation and the visceral organs, and hypochondriasis, in which the patient complains of peculiar sensations in his body, such as changes in the shape and size of his head, and points them out to the physician as suggestive evidence of serious illness.

TREATMENT

After the condition with which one is dealing has been ascertained, the next step is to choose a suitable therapeutic procedure. The methods may be divided as follows: suggestion, especially hypnosis; reassurance; exploratory procedures in which one attempts to ascertain the distress under which the patient is expected to be laboring and tries to solve this problem with him; medicinal treatment; and, finally, guidance and care by social-service assistants. The exploratory procedures form by far the largest number. Because of the difficulties and skills involved in this method, it must often be delegated to a trained psychiatrist, who is familiar with the modes in which a person interacts to his environment, especially to other persons; yet it is essential for the general physician to know and use this procedure.

If a disorder is regarded as psychogenic it is considered to be due to conflicting stimuli arousing overwhelming emotions that the patient cannot handle with his own resources. The patient's symptoms, which to him represent disease, must be translated into a new context in which they will be recognized by both patient and psychiatrist as part of a disturbed emotional response to a difficult situation. Only if one succeeds in doing so, may the patient be successfully reassured about his illness, even though his difficulty may not be solved and even though he may feel upset. (Ross has given practical suggestions concerning how to do this successfully.¹²) Furthermore, only after the patient has found a solution of his predicament may he hope that his symptoms of anxiety and depression will disappear.

The successful completion of an exploratory procedure involves the discovery of a patient's predicament and a demonstration of its tangible solution. At first glance, this may appear a hopeless task. There is the necessity of winning over the patient for the psychiatric procedure and, after doing so, of making it possible for him to have free expression. Many failures occur at this point. Experience has shown that a number

of simple rules applying to the first interview may make all the difference between success and failure. The first of these is that the patient must believe that he is guaranteed reasonable privacy; this does not involve the privacy of a confessional. The patient is usually willing to waive this right if he knows how far his problems will be discussed and if he is assured of the bona fide interest of other listeners. Secondly, the patient must be assured that the physician has no moral bias and is willing to consider with him accounts even of events about which he feels very guilty or has broken taboos. Furthermore, the patient must be assured that the physician will not take advantage of him—that is, overrun him by authoritative advice when he would like to have an opportunity to make up his own mind. And, finally, the patient must have an opportunity to lead the way in the interview. This has led to a discarding of the ordinary systematic questioning in favor of a method by which material is collected in a somewhat erratic manner, following the lead of the patient and filling in the gaps as need be. Deutsch¹⁴ has described this procedure in great detail.

If these rules are observed and if one avoids compromising statements, not only may one succeed in obtaining the significant story of the patient's difficulty but also the solution may present itself to the patient without advice from the physician. In the presence of a trusted expert, the patient is likely to penetrate farther in his search for a solution, having stopped short at painful thoughts in his previous unaided ruminations.

It has been found desirable to separate this first step of the treatment into two phases: a brief preliminary interview, to get acquainted and to learn the essential complaint; and a second interview in which the patient is dealing with a known person with whom he may be confidential.

A frequent, false impression is that patients who have a large number of complaints and tell a great deal about their difficulties are the ones who benefit most. Much of the material may be quite insignificant. To understand which material is of consequence and which is not, some experience is needed in watching the patient's emotional response during the discussion, his hesitations and his labored efforts at communication. Apparently, only experiences that are described with some recurrence of emotion can be utilized for therapy. Of all the innumerable circumstances, it can be said that little turns out to have therapeutic moment except a situation that has aroused an overwhelming reaction of one of five major patterns of emotional response: grief in response to loss; anxiety in response to threat or temptation; rage in response to provocation; and the two

appetites, those of hunger for food and the need for sexual expression. The situation that aroused the emotion may be obvious or may become manifest only after considerable search. A person with hysteria of long duration may describe his life as free of stress and strain, and a person with an obvious anxiety neurosis may at first be completely unaware of any situation that should have aroused his rage or fear; yet it is always there, and if, after prolonged search, nothing along this line can be found, one is tempted to revoke the diagnosis and to consider seriously the presence of a structural or chemical disorder such as hyperthyroidism or a deficiency state.

The situation that arouses the abnormal response when once found may be strikingly simple and offer itself for easy remedy, as in the following case.

CASE 1. A 38-year-old fireman was referred 1½ years after he had fallen from a ladder and sustained minor hand injuries and a fracture of the right arm. Although the bone lesions had healed without defect, he was still complaining of pain in his arm and, in addition, had received compensation for nervous shock, symptoms of anxiety having developed about 4 weeks after the accident.

Exploration showed that this man had never had any serious illness, that he had in no way shown signs of "neurotic make-up," and he resented being questioned by a psychiatrist. It was discovered, however, that after the accident his superintendent had made arrangements to have him put on light duty and had given him a job as a telephone operator. Being accustomed to vigorous activity and to "showing off," he felt stifled. He then started to tell stories of former exploits and had to be repeatedly reprimanded by his superior. Being stalled from his usual activities, the patient became unduly irritated and had to refrain a good many times from outbursts of violence against the man who was guaranteeing him his compensation. Finally, the superintendent enclosed the telephone in a glass box, and thus effectively prevented him from any further verbal activity with his friends. It was then that the severe symptoms of anxiety developed.

With a knowledge of this state of affairs, it was obvious that the well-meaning rest cure had turned out to be the pathogenic agent and that winning the patient to attempts at renewed vigorous activity would be very likely to restore his equilibrium. He was advised to change his job and to apply for a position as probation officer, which he did successfully. At a subsequent visit 3 years later, he reported that he had been symptom free and that he had gladly given up his compensation for his new chance for enjoyable work.

Sudden, severe grief and sudden fright during accidents, as well as sudden prevention from the execution of an act of rage or an attempt to satisfy one's sexual urge, may be followed directly by a psychoneurosis. One is likelier to find, however, that a series of minor disturbances, to which the patient has not responded, may finally accumulate to such a degree that only a very violent or intense emotional reaction can offer adequate discharge.

CASE 2 A 27-year-old cranberry picker was referred 2½ years after sustaining a Pott's fracture of the right forearm while cranking a tractor. He complained of cramplike contractions of the muscles of the forearm, which led to a forced closure of his hand into a fist. Although his original fracture had healed, nervous symptoms had developed shortly after his return to work and he considered himself permanently disabled by this disorder.

Exploration showed that the cramp of the hand occurred only when the assistant superintendent was walking by, that the same assistant superintendent had ordered the patient, after hours, to crank the car an act that had produced the fracture and that this man had provoked him on innumerable occasions to violence. The patient had been unable to give in to these because he was on court parole for former brawls at the village tavern and had recently married a reformer wife who daily reminded him of his duty to keep his job for the sake of his child. He found to his own surprise that the cramp of his hand was really a fist about to be lunched against the hated assistant superintendent.

The symptom disappeared only after the company had given him a token advancement which somewhat improved his status in relation to the assistant superintendent.

Some such change in environment is often necessary to permit the patient to adjust himself without his symptoms. Even if the patient is willing to adjust himself to the situation again, a free saving device of some sort is necessary. Frequently, teamwork with a psychiatric social worker is indispensable to bring about this change which may be small indeed but which must exactly fit the patient's needs.

In the course of the exploration, it may become obvious that the patient habitually gets into situations that are very difficult for him to meet because of poor training or inadequate personality. If this is so, the simple exploration will not be satisfactory, and a more prolonged and effective method of altering the personality will be necessary. Patients with this type of condition must often be referred for psychoanalytic treatment. In severe conditions, such as hypochondriasis, it may be necessary to regard the patient as an object for care and guidance who may have to be looked after in a carefully planned family setting.

Fortunately, a large number of patients do not show any serious personality defect, but have developed their psychoneurotic inadequacy under the impact of a very difficult situation. If the situation is severe enough, the condition presented may constitute a psychiatric emergency, and special measures are indicated.

Under peacetime conditions, such measures are called for in the severe reactive depressions and the markedly incapacitating hysterical reactions with such symptoms as aphonia, paralysis and amnesia. In wartime these reactions occur in persons who witness violence and destruction and who should, with the greatest expediency, be re-

stored to their normal level of efficiency. For this purpose, a number of procedures have been developed, among which hypnosis finds its proper place. Hysterical monoplegias respond very well, as do states of anxiety after a severe traumatic experience. Hypnosis may be helped by the administration of sedatives, such as Pentobarbital and Sodium Amytal. Curiously enough, there is one other way of restoring such patients to proper functioning, by provoking in them an emotional reaction of the same degree as the previous traumatic reaction. This principle used to be applied by means of electric shocks, faradic current being employed, or by bringing the patient into frightening surroundings. These procedures have largely been abandoned. However, it may be advisable to use a chemical agent to produce a storm in the autonomic system.¹⁰ Thus, one may, to good advantage, give intramuscular injections of 20 to 25 mg of Mecholyl,¹ followed by appropriate commands for example, to make renewed efforts at using a paralyzed extremity and—even more important—to cease interfering, by undue contraction, with its proper functioning.

It is sometimes possible to use the emergency procedures as an opportunity for reliving the disturbing situations and for verbally expressing the emotional reaction connected with them. In this form, the so-called cathartic method initiated by Freud and Breuer has survived.

In most emergency procedures, however, one cannot get acquainted with the predicament. One pushes the patient back into a situation that once, at least, was intolerable for him. In war, this is inevitable, in peace, often enough, the situation has changed during the patient's hospital stay so that it has become more bearable.

However, in patients who are especially vulnerable,—that is, those who are especially easily aroused to overwhelming emotions,—one may have to use a procedure which confronts the person with the need for discussing repeatedly a disturbing situation that he has to meet. Freud discovered that recalling a painful experience is likely to bring with it a return of the emotion linked to this experience. This return is used in a skillful manner in psychoanalysis to 'desensitize' the patient and to steel him to cope with the ordinary occurrences that he will have to meet. Since some persons, owing to fear that they may have to meet difficult situations, have remained at an infantile level of emotional development and have missed a great many opportunities to strengthen and test their ability to withstand temptation and certain conflicts, psychotherapeutic procedures may well attain an educational value.

Numerous explorations have shown that a patient exposed to severe grief may temporarily be able to block his reaction in some manner. This reaction, however, may occur years later at the occasion of suffering a relatively innocuous loss. In other conditions, the emotional response may be delayed. It may also be distorted, and thus in grief a person who tries to extricate himself from his bondage to a deceased person may temporarily withdraw all his interest and may experience the world as unreal until his mourning is over.¹⁷ Since grief reactions, whether displaced or not, are usually self-limited, the task of the psychiatrist is often restricted to relieving the tension by mild sedation with Sodium Amytal or by stimulation with amphetamine (Benzedrine) sulfate.¹⁸ It may be pointed out that exploration can be performed only if the patient is not too much disturbed and if he is not too disinterested, and medical agents may be employed to maintain the most suitable level of emotional tension; thus, it is futile to discuss with a severely depressed patient the reason for his mourning.

One of the most striking depressive reactions, with agitation, insomnia, restlessness and hopelessness, is often found after surgery, particularly after pelvic operations in women, after tooth extractions and after eye operations.¹⁹ This reaction is not likely to occur before a free interval of four weeks, and may then go on for years, the patient being entirely unaware of the situation that has aroused the overwhelming emotion. Exploratory therapy tracing back the emotional response has led to the discovery that the rage response is the outstanding reaction. If the patient is helped to handle his unwarranted rage, readjustment occurs with surprising ease. A number of middle-aged women who were considered to suffer from melancholia have responded to this form of psychotherapy with enduring success after four or five interviews.

RESULTS

This review of methods may be augmented by a report about follow-up observations. Such observations are admittedly difficult because they depend on the goal that one has placed before oneself. Also, the reports of the patients and their families are often unreliable. One may, however, obtain a rough estimate if one agrees that treatment should be regarded as successful with patients who feel satisfied, are able to work and who are not handicapped in their social and sexual adjustment.²⁰ If they still have their symptoms but do not let them interfere with their work, they should be considered improved only. Everything else, for the purposes under discussion, has been considered failure.

Of 200 patients who were seen between October 1, 1937, and October 1, 1939, in the Psychiatric Out Patient Clinic of the Massachusetts General Hospital, and who were seen again a year after discharge, 162 were satisfied, and 38 considered the treatment a failure. These good results may partly be due to the fact that we selected patients who, experience had shown, would respond to treatment. In the progress of our work, we began to realize that the anxiety states, the reactive depressions and hysteria were suitable for the type of therapy available in our clinic.

The treatment of hypochondriasis proved unsuccessful in almost every case; obsessive neuroses improved only temporarily.

The patients with anxiety neuroses turned out much better. The explorative technic was used on all of them; some lost their symptoms after only one interview, and others, especially those who had phobias, had to have more than fifteen interviews. Several anxiety neuroses were temporarily relieved by amphetamine; some of them responded with a paradox reaction, becoming much worse.

The care of patients with depression was very successful, but it is suspected that some of the anxiety neuroses that had a depressive coloring improved not so much because of our efforts as because of the self-limiting character of a depressive reaction.

The patients with hysteria showed a mixed picture. Severe hysteria, with a history of longstanding infantilism and typical hysterical personality, does not respond well to general hospital psychotherapy. This seems to be the domain of the prolonged treatment and psychoanalysis, which may succeed with some patients when other methods fail, but even this procedure does not always guarantee success. Patients with hysteria who have undergone a large number of operations are also difficult; we have failed in almost every one of them. On the other hand, patients with limited hysterical symptoms, such as monoplegias, may lose their symptoms after one or two interviews or in response to one of the more forceful procedures, such as hypnosis or the use of Mecholyl.

If our findings are compared with those in other reports, it is noted that the recovery rate with systematic treatment varies but little from clinic to clinic, and that the percentages of recovery or marked improvement are reported as 70, 82 and 87.²¹ This looks very encouraging, but one must take into account the natural recovery rate of the psychoneuroses. Landis²² has collected statistical data from numerous hospital sources and has stated that 62 psychoneurotic patients out of every 100 are discharged from state hospitals within a

year. This, of course, does not mean that they are recovered or symptom free but rather that they have been able to be returned home. Controlled series of an adequate sort giving a natural history of the neuroses are not available as yet

* * *

It is possible to learn psychotherapy. Physicians in training witness interviews for about a month and then do explorative work themselves with patients, discussing each interview with an older man. From this experience, they become acquainted with the pitfalls of the methods and avoid the two most serious dangers of psychotherapy: getting involved in the patient's emotional reaction to the therapist and driving the patient into "acting out," in his social life, primitive reactions that may have been discussed in the interview. In consequence of these reactions, a poor psychiatrist may be as dangerous for a patient's social life as a poor surgeon for his physical life. A young physician who is not at all suited for psychotherapy very soon becomes bored with it. A certain amount of ability to listen and a capacity to let the other fellow have his say are prerequisites for this work.

In our clinic, in addition to young psychiatrists in apprenticeship, we also train a number of physicians whose primary interest is in medicine rather than in psychiatry but who want to be able to use psychotherapeutic methods intelligently in general practice and to learn to recognize cases that should be referred to a specialist for more intensive treatment.

At present, the war situation and the intensified requirements of industry, in which every loss of efficiency due to neurosis counts double, require

more than ever the psychotherapeutic efforts of the general practitioner. One of the most challenging problems is presented by the 8 to 11 out of every 100 selectees who are now being rejected because of psychiatric difficulties, for whom methods of rehabilitation are being sought.

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CLINICAL FEATURES OF PANCREATIC LITHIASIS*

Report of Two Cases

ROBERT E. MOSS, M.D.,† AND EDWARD D. FREIS, M.D.‡

BOSTON

THE formation of stones in the pancreas has been recognized since 1667. The presence of stones in the pancreas of a patient with diabetes was first reported in 1788,¹ when a direct relation between pancreatic stones and diabetes mellitus was suggested. Further interest in this relation was aroused in 1901, when Opie² stated that stones may lead to atrophy of the pancreatic parenchyma, although the islet cells are not affected. In 1920, Barron³ pointed out that atrophy of the pancreas, resulting from long-continued obstruction of the ducts by stones, is not associated with diabetes mellitus provided that the islands of Langerhans remain intact. This observation served as the stimulus for the work that resulted in the discovery of insulin.¹

Despite the long history of the subject and its potential importance, it has generally been believed that pancreatic lithiasis is relatively rare. That this is not entirely true is shown by a few recent reports. In 1936, Mayo⁴ found 25 cases listed in the records of the Mayo Clinic, and in the next four years, Snell and Comfort,⁵ conducting a systematic search, discovered 18 additional cases. Opie,⁶ in 1500 necropsies, observed only 2 cases of pancreatic stones, and Dillon⁷ found only 2 among 2800 autopsy records. Lüdin,⁸ on the other hand, by very careful examination of each pancreas, noted 28 cases in a series of 542 autopsies. Warren⁹ reported a frequency of 3 cases in an autopsied series of 300 patients with diabetes. Smith and Bonis¹⁰ found, in the course of five months, 3 cases in a series of 240 roentgenologic examinations that included the pancreatic area. Finally, Rockwern and Snively¹ saw 2 cases within a month at the Cincinnati General Hospital, although only 3 had occurred among 7402 post-mortem examinations at that hospital in the preceding twelve years.

More and more cases are being diagnosed during life as the value of taking a flat film of the abdomen in patients with abdominal pain gains wider appreciation. It has been pointed out, however, that a barium meal can easily obscure the presence of pancreatic stones.¹ At the Boston City Hospital, the diagnosis was made in 3 cases from

1934 to 1941—at operation in 2 and at autopsy in 1. During 1941, 3 cases of pancreatic stones were recognized among 700 autopsies. Two additional cases were observed while on the wards of this hospital at the same time. The diagnosis in one rested on the roentgenogram; in the other, the roentgenographic findings were confirmed by palpation of the pancreas at laparotomy. Because we were able to study the pancreatic ferments of these patients before and after stimulation with Mecholyl (acetyl-beta-methylcholine chloride) and because few cases have been studied with the aid of such pancreatic stimulants as secretin and Mecholyl, we believe that our data warrant reporting.

To obtain the duodenal juice uncontaminated by gastric juice, the method described by Agren and Lagerlöf¹¹ was used, care being taken to place the tube under direct fluoroscopic control. Mecholyl was used to stimulate the external pancreatic secretion according to the method of Comfort and Osterberg.^{12, 13} Amylase activity was determined by the method of Agren and Lagerlöf,¹¹ and lipase activity by that of Crandall and Cherry.¹⁴

CASE REPORTS

CASE 1. Mrs. J. B., a 35-year-old woman, was admitted to the hospital in July, 1941, complaining of pains in the legs, with weakness and inability to walk, of 2 months' duration. For 3 months, she had experienced anorexia, nausea and vomiting, especially in the morning, associated with more or less constant, but not usually severe, pain in the midepigastrium and left upper quadrant of the abdomen.

The patient had been admitted to this hospital in 1937, complaining of pains and weakness in the legs for a month and of midabdominal pain and vomiting for 6 days. Physical examination at that time revealed emaciation, scaling skin over the forearms, a beefy red tongue, an enlarged, firm, nontender liver, bilateral foot drop, absent tendon reflexes, loss of position and vibration sense, and tenderness of the calves. On a high intake of vitamins, carbohydrate and protein, the patient gradually improved over a period of 15 weeks. The discharge diagnoses were as follows: chronic alcoholism; alcoholic gastritis; dietary and vitamin B complex deficiency, with emaciation; polyneuritis; stomatitis; fatty infiltration of the liver; and chronic pyelonephritis.

Physical examination at the second admission showed marked emaciation, a strong odor of alcohol, tremors of the hands, roughening and scaling of the skin, particularly over the dorsum of the hands and over the elbows, and multiple ecchymoses over the extremities. The tongue was smooth and red. The liver edge was firm, smooth and sharp, and was palpable 3 cm. below the costal margin. The abdomen was soft and extremely tender in the left

*From the Evans Memorial, Massachusetts Memorial Hospitals, the Fifth and Sixth Medical Services (Boston University), Boston City Hospital, and the Department of Medicine, Boston University School of Medicine.

†Assistant in medicine, Boston University School of Medicine; resident physician, Evans Memorial, Massachusetts Memorial Hospitals.

‡Senior intern, Fifth and Sixth Medical Services (Boston University), Boston City Hospital.

upper quadrant. The feet were plantar flexed and could not be voluntarily dorsiflexed. All tendon reflexes were absent. The calf muscles were tender to pressure. The blood pressure was 120/80.

The blood Hinton reaction was negative. The red cell count was 2,700,000 with a hemoglobin of 9.8 gm and the white cell count was 9600 with a normal differential. The urine showed a specific gravity of 1.070, no albumin, sugar, acetone or casts and 10 white blood cells per high power field in the centrifuged sediment. The nonprotein nitrogen of the blood was 27 mg per 100 cc. The serum protein was 5.2 gm per 100 cc. The icteric index was 15. Urobilinogen was present in the urine in dilutions ranging from 1:20 to 1:40. The bromsulfalein excretion test of liver function showed 100 per cent retention at 5 minutes and 50 per cent retention at 15 minutes.

Because the patient developed an acute exacerbation of her chronic pyelonephritis during the 2nd week, a flat film of the abdomen was taken. No renal calculus was noted but irregular areas of calcification were revealed that extended across the upper abdomen, both to the right and to the left of the midline, at the level of the first and second lumbar vertebrae. These areas followed the general outline of the head and body of the pancreas (Fig. 1).



FIGURE 1 Case 1

This flat film of the upper abdomen shows many fine calculi in the tail, body and head of the pancreas.

and were later shown by gastrointestinal roentgenograms and by fluoroscopy during duodenal intubation to lie enclosed within the curve of the duodenum.

Determinations of the pancreatic enzymes, amylase and lipase, were carried out on two occasions, 19 days apart, by the methods noted above. The results are listed in Table 1. The serum lipase activity was 1.18 expressed in cubic centimeters of 0.05N sodium hydroxide (average activity ranges between 0.2 and 1.5 cc.). There was no diarrhea and examination of the stools stained with sudan III showed no increase in fat content. Glucose tolerance was determined with 100 gm of glucose by

mouth the values, expressed in milligrams of glucose per 100 cc of blood, were fasting, 83, 1 hour, 265, 2 hours, 274 and 3 hours, 263.

On a regimen consisting of a high carbohydrate, high protein and low fat diet, supplemented by brewers' yeast, thiamine hydrochloride, niacin (nicotinic acid), Vegex

TABLE 1 Results of Continuous Drainage of Fasting Duodenal Juice for One Hour before and One Hour after Mecholyl

DATA	VOLUME cc	AMYLASE gm of maltose	LIPASE cc of 0.05 N NaOH
Normal values			
Before Mecholyl	10-120	6-250	0-10,000
After Mecholyl	10-180	30-500	2000-18,000
Case 1			
Before Mecholyl	31 >4	3.6-18.8	490-1310
After Mecholyl	55-73	9.5-40.2	1,90-2490
Case 2			
Before Mecholyl	78-80	2.2-27.5	960-17.0
After Mecholyl	0-120	8.3-39.8	1360-25.0

and ferrous sulfate orally in addition to 5 cc of crude liver extract intramuscularly twice weekly the patient slowly improved over a period of 2 months. The liver receded to the costal margin, although she did not receive lipocae. The bromsulfalein test eventually showed 80 per cent retention of the dye at 5 minutes and 30 per cent at 15 minutes. A biopsy of the liver, obtained at this time with the peritoneoscope, revealed only minimal traces of fat in the parenchymal cells with minimal increase in fibrous tissue. The red cell count rose to 4,400,000 at the time of discharge.

CASE 2 Mrs G K, a 57 year-old woman was admitted to the Third Surgical Service (Boston University) of the hospital in September, 1941, because of three attacks of severe, colicky, right upper-quadrant abdominal pain with associated vomiting during the preceding 4 years. Between attacks, she had suffered from abdominal bloating and gaseous eructations after meals, particularly after spicy or fatty foods, and occasional mild diarrhea. During the year before admission she had noted polyuria, polydipsia and a weight loss of 35 pounds. Because glycosuria and hypertension, as well as pancreatic lithiasis by roentgenogram, were discovered, the patient was transferred to the Fifth Medical Service for further study prior to operation.

Physical examination showed her to be obese and not acutely ill. The renal arteries were narrow and tortuous, and the radial arteries were thickened. The heart was not remarkable. The blood pressure was 210/96. There was slight tenderness, but no spasm, in the right upper quadrant of the abdomen. The liver was not palpable.

The blood Hinton reaction was negative. The red-cell count was 4,500,000 with a hemoglobin of 12.2 gm (Sahli), and the white-cell count was 7000 with a normal differential. The urine showed a specific gravity of 1.035, no albumin, acetone or bile, an orange reduction with Benedict's solution, and 1 hyaline cast and 2 white blood cells per high power field in the centrifuged sediment. The nonprotein nitrogen of the blood was 30 mg per 100 cc, and the fasting blood sugar 143 mg. The icteric index was 5. Urobilinogen was present in the urine in a dilution of 1:16. The bromsulfalein excretion test showed 45 per cent retention at 5 minutes and 5 per cent retention at 15 minutes.

A Graham test showed poor filling of the gall bladder with dye and failure to empty after a fatty meal.

roentgenogram of the abdomen revealed several areas of calcification in the region of the head of the pancreas (Fig. 2).

Two determinations of pancreatic enzymes were performed 13 days apart. The results are recorded in Table 1. Stools stained with sudan III showed no excess of fat.

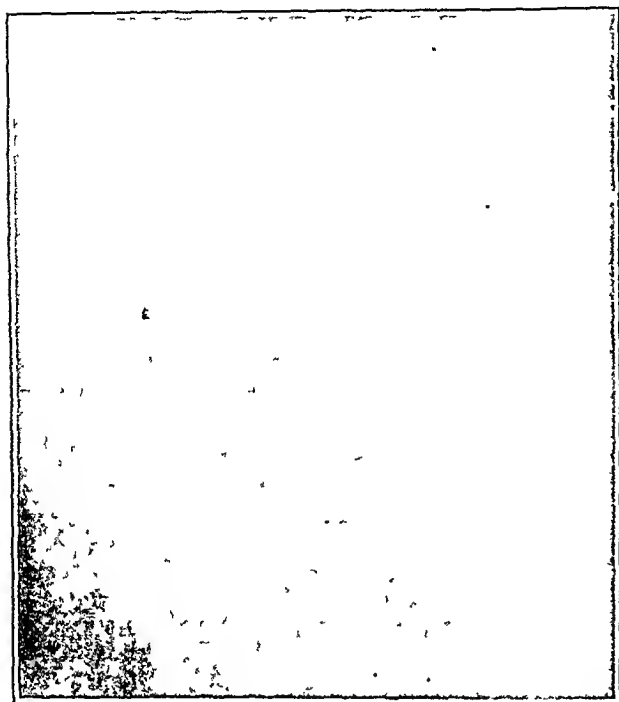


FIGURE 2. Case 2.

This lateral film of the upper abdomen shows two large calculi in the head of the pancreas.

While under observation, the patient had a severe attack of right-upper-quadrant colic, accompanied by fever and leukocytosis. The serum lipase during the attack was not elevated (0.73 cc. 0.05N sodium hydroxide).

After completion of studies and control of the diabetes by diet and 25 units of protamine zinc insulin daily, the patient was returned to the Third Surgical Service. Operation disclosed a large stone in the gall bladder, with a small stone and some gravel in the common bile duct. The liver appeared normal, and no biopsy was taken. The pancreas was not visualized. By palpation, however, it was considered to be atrophic, and several stones were easily palpable. No attempt was made to remove them.

DISCUSSION

The origin of pancreatic stones is not entirely clear. Because they consist of calcium carbonate and tribasic calcium phosphate, which are not present in normal pancreatic juice,⁵ and because bacteria have been found in them,¹⁵ it is generally assumed that infection of the pancreas causes an alteration in the juice, leading to the deposition of calcium salts.^{5, 15, 16} In addition, stasis of the secretions in the ducts appears to be necessary, as Lazarus¹⁷ found that stones could be produced in the pancreas of dogs only by a combination of stasis and infection. From this evidence, it has been inferred that pancreatitis and, possibly, cho-

lecystitis and cholelithiasis are the major predisposing causes of the disease. However, few cases have a history of previous attacks of pancreatitis. There was no conclusive evidence that either of the patients in the cases presented above had ever suffered from acute pancreatitis, although the mild abdominal pain and vomiting noted in Case 1 at the first admission could have had such a basis.

Many patients, however, show a coexisting cholelithiasis, although Snell and Comfort⁵ found only 3 in their series of 18 cases. One of our patients (Case 2) had associated cholecystitis and cholelithiasis; the other had no definite symptoms of gall-bladder disease and showed no cholesterol or calcium bilirubinate crystals in the "B" bile obtained by duodenal drainage. Although evidence of cholelithiasis or pancreatitis cannot be ascertained clinically in many cases, at post-mortem examination the pancreas is frequently the seat of an inflammatory process that may be evidenced only by fibrosis and cystic changes at the time of examination.

The clinical diagnosis, although difficult, is probably often missed because it is not thought of. Upper abdominal pain is usually the leading symptom, varying from mild distress to severe colic that resembles biliary colic. However, it is likelier to be referred to the left side of the abdomen and may radiate to the left side of the back, to the left costovertebral angle or to the left shoulder.⁵ Nausea and vomiting may be severe. Attacks seem to be induced by fatty foods, but are more frequently precipitated by alcoholic excesses than attacks of gallstone colic.¹⁵ *Fatty diarrhea* is perhaps the most characteristic sign of the disease, but it has been noted in no more than half the reported cases and may be intermittent, occurring only after an episode of colic.⁵ Enlargement of the liver may be another late sign of pancreatic damage. The work of Dragstedt et al.¹⁸ suggests that this results from fatty changes in the liver consequent to deficient production of lipocaiic by the pancreas. Diabetes mellitus, actual or latent, accompanied by abdominal pain of obscure origin, should immediately point to the possible existence of this disease. Finally, icterus occasionally occurs in pancreatic lithiasis. If this syndrome is kept in mind and a flat film of the abdomen is obtained in suspected cases, the diagnosis should be made with greater frequency.

The chief difficulty in the clinical diagnosis of pancreatic stones lies in the frequent absence of unmistakable signs of pancreatic insufficiency. Coffey, Mann and Bollman¹⁹ have shown experimentally with dogs that gross alterations of digestion as manifested by steatorrhea and creatorrhea, occur only in the complete absence of the external pa-

creatic secretion from the intestine. Even small amounts of pancreatic tissue sufficed to maintain complete digestion in their animals. To facilitate the diagnosis of relative pancreatic insufficiency, when steatorrhea is absent, Agren and Lagerlof¹¹ using secretin, and Comfort and Osterberg,¹²⁻¹³ using secretin and Mecholyl as pancreatic stimulants, describe methods for obtaining the external pancreatic secretion uncontaminated by gastric juice. The procedures give a roughly quantitative estimate of pancreatic output.

We used Mecholyl in studying the pancreatic enzyme production of our patients. Each patient was examined on two separate occasions, since we have found that one test may give misleading low results that cannot be duplicated later. Table 1 shows that the amylase and lipase contents of the duodenal juices of both patients were in the low normal range. In each case, there was a significant increase in enzyme content after stimulation with Mecholyl, the only exception being the first lipase determination in Case 2. The results of these tests indicate that some pancreatic damage was present, yet not enough to lead to gross steatorrhea. The conclusion appears legitimate that the damage was directly connected with the calculi present, which caused obstruction of the ducts with resulting atrophy of the acinar tissue. Lagerlof,¹⁰ Snell and Comfort,⁴ Smith and Bonis¹⁰ and Rockwern and Snively¹ found normal or low amounts of enzymes in their patients with pancreatic lithiasis.

Reference has already been made to the frequent finding of diabetes mellitus in association with pancreatic stones. Since the incidence of diabetes is greater in cases of longer standing, the implication is that it results from progressive destruction of the islets of Langerhans. However, it is remarkable that there may be no correlation between the degree of pancreatic damage and the severity of the diabetes. In fact, patients who appear to have extensive pancreatic destruction over a long period may show no sign of diabetes. Opie² commented on the case of a ninety year old man who had been in good health all his life despite the presence of steatorrhea for twenty years prior to his death; the patient had no symptoms or signs of diabetes yet, at autopsy, the duct of Wirsung was completely blocked by a calculus, and the pancreas was almost wholly replaced by fat. Another man, who was 72 years old, had had fatty diarrhea for two years, but never had had glycosuria; the pancreas was entirely replaced by fat, with a large stone in the duct and smaller ones scattered throughout the gland. In a third case of pancreatic lithiasis, seen on the Third Medical Service of the Boston City Hospital before the cases presented above, the

patient was a known diabetic who had been controlled for a year by 15 units of protamine zinc insulin. He gradually failed, complaining of mid abdominal pain radiating into his left upper quadrant and back. The diabetes, during his final sojourn in the hospital, became less severe and was eventually controlled by 5 units of protamine zinc insulin daily. At autopsy, however, the pancreatic parenchyma was found to be about 95 per cent destroyed, being replaced by chronic inflammatory tissue and cystic, dilated ducts containing many irregular, rough stones.

So far as the enlarged liver that may be a late accompaniment of pancreatic lithiasis is concerned, we wish to point out that the patient in Case 1 showed a definitely enlarged liver, with decreased function of the bromsulfalein test. She was treated with a low fat, high-carbohydrate, high protein diet and a high vitamin intake, rather than with lipocac. Response to this regimen was quite satisfactory. The liver gradually receded to normal size, and a post treatment biopsy showed only minimal amounts of fat and fibrosis. We concluded that the hepatic enlargement in this case was not due to lipocac deficiency.

Although no attempt was made to remove the stones in either of our patients, surgery has frequently been employed successfully both to rid the patient of symptoms and to halt further destruction of the pancreas. Of 65 cases collected from the literature, 58 were treated surgically.¹⁴ Schmieden and Sebening²¹ call attention to 11 patients who were completely cured by removal of the stones. At the Mayo Clinic, when the diagnosis had been made sufficiently early, successful operations were performed.⁵ The danger of postoperative pancreatic fistulas has been largely overcome by improved surgical technique, and reactivation of the pancreatitis or peritonitis appears to be rare.

In the symptomatic treatment of the disease, the use of dried pancreatic juice to correct the symptoms of pancreatic insufficiency has been of value. Although the fatty liver in Case 1 did not require lipocac, Snell and Comfort found that it had a specific effect in at least 1 of their cases. The colic is usually treated with morphine, but ephedrine is worthy of a trial, since it diminishes pancreatic secretion. The primary treatment of this disease, however, is surgical.

SUMMARY

Recent reports agree that pancreatic lithiasis is not excessively rare. The clinical diagnosis is becoming more frequent as roentgenograms of the abdomen are more widely obtained in cases of obscure abdominal pain.

Two cases are reported in which the diagnosis was made during life by roentgenography and confirmed in 1 case at operation. The degree of pancreatic insufficiency was determined by examination of the enzyme activity of the duodenal contents after stimulation with Mecholyl. Lipase and amylase activity fell in the low normal range. Steatorrhea was not present. One patient had cholelithiasis and frank diabetes mellitus. The other had a decreased glucose tolerance and an enlarged liver that showed improvement without the use of lipocaic.

The essential features of pancreatic lithiasis are discussed.

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MEDICAL PROGRESS

DISEASES OF THE THYROID GLAND

J. H. MEANS, M.D.*

BOSTON

SINCE my first report on this subject of three years ago,¹ a large amount of investigative work, both experimental and clinical, has been reported and must needs be digested. The large volume of such work is in part owing to the fact that many new approaches to the study of thyroid physiology, both normal and morbid, have recently become available.

For many years, one looked upon basal metabolic rate as the sole yardstick for measuring thyroid function. Then the determination of blood iodine levels made its appearance on the scene, and now such procedures as the measurement of thyrotropic hormone output in the urine, the collection of radioactive iodine by the thyroid, the effect of patients' serum upon the metabolism of test tissues, thyroid or other, the behavior of patients' thyroid when explanted in tissue culture and many other methods are available to him who would solve a hormonal riddle.

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*Jackson Professor of Clinical Medicine, Harvard University, chief, Medical Services, Massachusetts General Hospital.

A report on progress in diseases of the thyroid gland in this year 1942 may properly take its departure from the thyrotropic hormone of the anterior pituitary, or as it is convenient to call it, TSH (thyroid stimulating hormone), because this hormone still is a center of interest, and the discovery of how it acts on the thyroid cells may elucidate some of the morbid hormonal patterns encountered in thyroid diseases.

To the reader interested in being brought up to date on the now vast literature on TSH, the article of the Australian, Lambie,² can be most heartily recommended. Lambie reviews the literature, giving a bibliography of three hundred and nine titles, and also reports observations of his own and discusses the relation of the hormone in question to clinical syndromes. He draws the broad general conclusion that the ultimate stimulus to the thyroid is chemical, not nervous, but this does not mean that nervous influences may not impinge on the thyroid, nerve-borne from hypothalamus to pituitary, humorally from pituitary to thyroid. With this concept, I find myself in substantial agreement. It provides an explanation

for the paradox that whereas disturbed thyroid function may follow psychic trauma, experimental evidence is against any direct secretory innervation of the thyroid gland (Uotila¹)

That a hormonal balance exists between pituitary and thyroid was indicated in my previous review.¹ Salter⁴ has given this the appropriate name of "pituitary thyroid axis," a beneficent axis in health, but sometimes leading to mischief in disease, like a certain other axis, which need not be mentioned. The evidence that the pituitary through its TSH drives the thyroid cells to increased activity is so abundantly proven as to need no further discussion, and DeRobertis⁵ has shown that changes in thyroid histology begin as early as fifteen minutes after the injection of TSH.

The evidence that the thyroid hormone inhibits the pituitary with respect to TSH secretion is also increasing (Reforzo Membrives,⁶⁻⁸ Uotila⁹ and Friedgood, Bevin and Uotila¹⁰). Reforzo Membrives, for example, claims not only that the pituitary glands of rats fed with thyroid fail to maintain the thyroid gland of pituitarectomized rats, but also that the thyroid glands of such rats showed an even more pronounced atrophy than those of pituitarectomized rats that had not received thyroid. In other words, the pituitary glands of rats long treated with thyroid had a depressing instead of a stimulating action on the thyroid glands of pituitarectomized rats.

The precise mode of action of TSH on the thyroid is now the subject of lively study. Collip¹¹ cites Eitel et al.¹² as having shown that TSH acts directly on the gland, not through an intermediary. Galli Mainini¹³ has confirmed this. Collip further cites Schneider and Widmann¹⁴ as having demonstrated that TSH will cause symptoms of thyrotoxicosis faster than thyroxine, which suggests that it cannot be considered merely as a liberator of thyroxine. However, the explanation for this relation may be that thyroxine after administration has to be altered in its molecular structure before becoming physiologically active, and that this process requires time, whereas the thyroid when stimulated by TSH puts out its hormone in more immediately available form.

Indeed, the whole problem of the form in which hormones are secreted and act on their end-organs is important but not well understood. Chow, Greep and van Dyke¹⁵ have treated various hormones with various enzymes and apparently have shown that when TSH is broken down enzymically below the protein level, it ceases to exert a hormonal effect. It is really unknown in what form thyroid hormone is carried in the blood and in what form it exerts its end-organ effect. It is stored in the follicle in a form which DeRobertis¹⁶ describes as an optically homogeneous,

highly viscous, refractile fluid (colloid). Its viscosity, he finds, diminishes after the injection of TSH and for a short period after the administration of potassium iodide. After a longer period on iodide, the viscosity of colloid increases. It is extremely interesting that DeRobertis was able to demonstrate in colloid obtained from single follicles a proteolytic enzyme which digests a gelatin substrate. This observation is interesting in connection with the work of Salter and Pearson,¹⁷ which showed that thyroid proteins can be synthesized enzymically. The thyroid hormone, however, does not appear to circulate as a protein, at least not as thyroglobulin, for Lerman,¹⁸ precipitating with thyroglobulin immune serum, could find none in the circulating blood in hyperthyroidism, hypothyroidism or euthyroidism. It may be broken down again enzymically between thyroid cell or follicle and end organ. Indeed, hormone physiology is rapidly entering the realm of enzyme chemistry.

TSH is also somewhat elusive when searched for in body fluids, but less so than thyroid hormone. Hertz and Oastler¹⁹ found evidence of thyrotropic activity in the blood and urine of myxedematous patients, but not in that of thyrotoxic or normal subjects. Rawson and Starr²⁰ demonstrated large quantities of TSH in the urine of totally thyroidectomized patients and failed to recover it from the urine of thyrotoxic ones. In the urine of normal young men, evidence of some thyrotropic activity was obtained, but much less than in that of those who had been thyroidectomized. Bastenie²¹ has also found thyrotropic activity in the urine in certain cases of myxedema. Robinson²² studied the bloods of patients with various sorts of thyroid disease, including myxedema and thyrotoxicosis, and was unable to demonstrate a thyrotropic effect in any of them. Collip, Mills, Rundle and Sharpey-Schafer²³ also searched for TSH in the blood in normal subjects; they could find none, even after the injection of TSH at a time when the subjects were thyrotoxic from this injection. In thyrotoxicosis, they got positive assays in 4 out of 15 cases. Positive assays were also obtained in spontaneous and postoperative myxedema and in patients with severe proptosis and ophthalmoplegia, as discussed below. Loefer²⁴ injected large amounts of TSH into the blood stream of rabbits and was able to detect it for only thirty minutes after injection in the intact animal, but for much longer periods in the thyroidectomized one. Seidlin,²⁵ in a similar study, observed TSH in the urine of thyroidectomized guinea pigs that had been injected with large amounts of TSH, but could not recover it after injection into normal guinea pigs. Observa-

tions of this character raise the question whether the thyroid gland removes TSH from the blood stream or in some way inactivates it. Rawson, Sterne and Aub²⁶ reported that TSH, when exposed to tissue cultures of normal rabbit thyroid, lost its physiologic activity, but that no other tissue had this property except thymus and lymphatic tissue. These investigators further found that thyrotropic activity could be restored if the medium was heated in a sealed vessel at 100°C. for one hour. About 80 per cent of the original thyrotropic activity, which had been completely lost during exposure of the medium to thyroid tissue, could be recovered in this fashion. Furthermore, it was found that thyrotropic activity can be found in heated urine when it appears to be absent before heating. These observations, undoubtedly extremely important, indicate that the thyroid gland inactivates TSH, but does not remove it from the blood stream, and that somehow or other, in this process of inactivating TSH, the thyroid parenchyma receives a stimulus which causes it to become hyperplastic and to increase its secretion of thyroid hormone. This is essentially the conclusion also of Collard and his collaborators.²³

The morbid physiology as found in the thyrotoxicosis of Graves's disease may well be due not to an increased secretion of TSH by the pituitary, but to an increased sensitivity of the thyroid cells to TSH. The work of Stephens²⁷ supports such a view. He placed guinea pigs on starvation diets and observed that the thyroids of such animals became atrophic, but also that such thyroids were many times more sensitive to TSH than those of normally fed animals. These results suggest that the observations of Hertz and Means²⁸ and Andersen²⁹—that severe weight loss, with or without thyroid therapy, sometimes precipitates thyrotoxicosis—may also be explained on the basis of hypersensitivity of the thyroid to TSH action. Friedgood, Bevin and Uotila¹⁰ have also shown that the effect of TSH is significantly enhanced by adrenalin and by pilocarpine. They suggest that pilocarpine acts through the adrenal medulla and that adrenalin makes thyroid cells more sensitive to TSH. This brings to mind the once well-known Goetsch test.

The nature of the hormonal imbalance in various clinical syndromes has been studied by Galli-Mainini.³⁰ This investigator exposed normal guinea-pig thyroid to patients' serum in the Warburg apparatus and noted the effect on the oxygen absorption of the tissue (QO_2). For control, guinea-pig thyroid was exposed to normal human serum and the result was expressed as the percentage variation of the QO_2 of thyroid in patients' serum from that in normal serum. Such a procedure discloses whether the hormonal action

of a patient's serum is more or less thyroid-stimulating or thyroid-depressing than is that of a healthy person. Presumably, it shows whether thyrotropic activity of the pituitary or pituitary-depressant activity of the thyroid is in the ascendency. Of course, the activity of antihormones of various sorts may enter the picture. In classic Graves's disease, Galli-Mainini found evidence of an excess, relative or absolute (presumably the latter because the basal metabolic rate is elevated), of thyroid hormone activity. By thyroidectomy this was corrected. There was an excess of thyrotropic activity in acromegaly and also in those peculiar cases of Graves's disease which Means, Hertz and Williams³¹ and Means³² have called Graves's disease with dissociation of thyrotoxicosis and ophthalmopathy, or a special ophthalmic type of Graves's disease. In untreated primary myxedema, there was an elevation in QO_2 , and in treated cases, there was a slight elevation in two and reduction in two others. This separation of Graves's disease into two types is further discussed below.

With regard to the finding in acromegaly, it is of interest that Davis³³ found the thyroid enlarged in 50 per cent of a series of 166 cases of acromegaly, and for contrast with this, we may recall that it has been known since 1851 that the pituitary is hyperplastic in cretinism (Nièpce³⁴) and since 1889 that it shows changes after thyroidectomy (Rogowitsch³⁵). In other words, in acromegaly, the enlarged pituitary may stimulate the thyroid; in hyperthyroidism, the lack of thyroid secretion may stimulate the pituitary.

There are other humoral agents than TSH which affect the function of the thyroid. Iodine is, of course, the time-honored one. The endocrine function of iodine has been made the subject of exhaustive critical review in two recent monographs (Elmer³⁶ and Salter⁴), to which the reader is enthusiastically referred. That iodine inhibits or counteracts the thyrotoxicosis induced by TSH administration, much as it does the spontaneous thyrotoxicosis of Graves's disease, is well established. Salter points out that such action may be either directly on the thyroid, on the anterior pituitary and its TSH, or on end organs peripherally. Salter and Lerman³⁷ have discussed the first of these as a mass action due to increased iodine concentration, which favors the storage of thyroid protein. Some writers, notably Marine,³⁸ believe that thyroid function is totally dependent on the pituitary, but the work of Chapman^{39, 40} indicates that the thyroid can respond with increase in parenchymal-cell height to iodine lack in pituitarectomized animals, and Vanderlaan, Vanderlaan and Logan,⁴¹ studying the QO_2 of animals to which

TSH was given with and without iodine, reached the conclusion that iodine acts directly to inhibit the metabolic activity of the thyroid. On the other hand, Chapman has found a physiologic action of iodine in animals without thyroids. This appeared in experiments in which it was shown that although the level of iodine intake does not affect the growth curves of intact animals, there was less weight loss in thyroidectomized animals on high iodine intakes than in those on low. Chapman suggested the possibility of the production of a thyroxinelike material in the tissues. In any event, it seems likely that the action of iodine on the pituitary-thyroid axis may be on more than one front.

As has become increasingly apparent recently, other chemical agents than iodine may exert a seemingly specific effect on the thyroid, or on the pituitary-thyroid axis. Since the work of Hunt⁴² in 1905 and of Chesney, Clawson and Webster⁴³ in 1928, it has been known that cyanides and vegetables containing these may be goitrogenic. Rawson, Hertz and Means⁴⁴ reported the case of a man who, after a year's treatment with potassium sulfocyanate for hypertension, rapidly developed the following weird syndrome: hyperplastic goiter with loud bruit, hypothyroidism, exophthalmos and blood iodine at the myxedema level. His thyroid promptly reverted to normal size, and his hypothyroidism disappeared merely on omission of sulfocyanate. The biopsy showed a wildly hyperplastic thyroid—hyperplastic but impotent, because his general state showed that he was suffering from a shortage of thyroid hormone. Kobacker⁴⁵ has reported a similar case, in which the picture went to that of full-blown myxedema. Kobacker's patient recovered on omission of sulfocyanate and exhibition of thyroid, but a year later, when sulfocyanate was resumed, the myxedema recurred. Dr. Herrman L. Blumgart tells me that a similar case has been observed at the Beth Israel Hospital, Boston, and from the Mayo Clinic (Fahlund⁴⁶) comes the report of a patient who developed what appeared to be acute thyroiditis as a result of sulfocyanate therapy for hypertension.

At the same time that these human cases in which sulfocyanates had had a significant effect on the thyroid gland were being studied, experimental work was appearing indicating that the sulfonamide drugs and other sulfur-containing substances may also cause thyroid hyperplasia (MacKenzie and MacKenzie,⁴⁷ Astwood⁴⁸ and Richter and Clisby⁴⁹). Thus, not only do cyanides and cyanates appear to be goitrogenic, but also a group of substances containing sulfur. The role of sulfur in the economy of the thyroid gland becomes interesting. One point of difference between

cyanide or cyanate thyroid hyperplasia and that caused by the sulfonamides is that the former is preventable by the administration of iodine while the latter is not preventable by this means.

How these agents work on the thyroid gland is of great interest but not settled. Do they act through TSH, directly on thyroid cells, or on the end organs of the thyroid hormone? The last-mentioned theory has been widely held but at the present writing seems unlikely. A group of New Zealanders has done significant work on this question (Kennedy and Purves,⁵⁰ Griesbach⁵¹ and Griesbach, Kennedy and Purves⁵²). These investigators caused goiter in rats by feeding seeds of the Brassica (cabbage) family of plants. The goitrogenic agent is presumably a cyanide of some sort. It was found that these seeds were highly goitrogenic, producing a clearly hyperplastic type of thyroid gland in intact animals, but had no such effect in hypophysectomized rats. Also, thyroid hyperplasia caused by feeding of the Brassica seed regressed after hypophysectomy, despite the continued administration of the seed. From these results, the authors concluded that the active principle of Brassica seeds cannot stimulate the thyroid gland directly, but requires the mediation of the thyrotropic hormone. They were also able to show that certain changes occur in the anterior pituitary glands of Brassica-fed rats—namely, a rapid increase in basophilic cells and a simultaneous loss of acidophilic cells. They concluded that the basophilic cells are the source of TSH. Sharpless and Hopson⁵³ had previously found quite similar changes in soybean-fed rats. Iodine or desiccated thyroid increased the proportion of acidophils and decreased the proportion of basophils, but only thyroid produced the normal percentage of basophils.

Whether any practical application to treatment will arise from these experiences with cyanides, cyanates, sulfonamides and so forth, it is impossible to say at present. In any event, it is worth the physician's while to know that sulfocyanate administration can cause goiter and hypothyroidism and that thyroid or iodine will prevent or control it; and also it can be said that the information is of great scientific interest, and may provide a new approach to the study of the pituitary-thyroid axis, or of the relation between the thyroid gland and its end organs, the cells of the body.

The relation between vitamins and thyroid and other endocrine activity is being given considerable attention. Carrière, Morel and Gineste⁵⁴ have studied the effect of both excess and deficiency of various vitamins on the thyroid gland in guinea pigs. An excess of either vitamin A or C was

found to inhibit the gland, an excess of vitamin B to stimulate and an excess of vitamin D still further to stimulate. It was concluded that vitamins A and C may be helpful in hyperthyroidism, but that vitamin D and heliotherapy are contraindicated. The action of vitamin B in these experiments is of academic interest only because there is abundant evidence that this vitamin is helpful in the treatment of thyrotoxicosis (Means, Hertz and Lerman,⁵⁵ Frazier, Brown and Vars⁵⁶ and Bickel⁵⁷). Wohl and Feldman⁵⁸ suggest that hyperthyroidism destroys and depletes vitamin A reserves in the body. This is evidenced by pathologic dark adaption in 18 out of 20 patients with thyrotoxicosis. Azerad⁵⁹ also gathered evidence of the same sort and concluded that vitamin A may be useful in thyrotoxicosis.

Thyroid-gonad interrelations also awake some interest. Nathanson, Brues and Rawson⁶⁰ found that testosterone propionate is capable of stimulating the thyroid and parathyroid glands of the intact immature female rat. It is not clear whether this is a direct effect or one routed through the pituitary gland; the latter was thought more likely.

Estrogenic substances have been tried in the treatment of thyrotoxicosis, with, on the whole, conflicting results. Robinson⁶¹ treated 5 patients with primary Graves's disease and 2 with toxic adenoma with massive doses of Progynon B, without success except in a menopausal case in which the relation of the result to therapy given was uncertain. Goldman, Goldman and Kurzrok,⁶² on the other hand, treated 8 women with hyperthyroidism with large doses of Progynon B. Five of these patients were at the menopause, and all showed improvement. These authors conclude that some cases of menopausal thyrotoxicosis respond favorably to treatment with estrogenic hormone.

In the radioactive iodine approach to thyroid physiology and therapeutics, progress continues to be made. After studying the uptake of iodine by the thyroid gland under a variety of experimental and clinical conditions, Hertz and Roberts⁶³ have recently made use of radioactive iodine in the treatment of thyrotoxicosis, with some encouraging results. Hamilton and Lawrence⁶⁴ have also reported results in 3 cases. Since the original paper on the use of radio-active iodine in the study of thyroid physiology by Hertz, Roberts and Evans,⁶⁵ a considerable literature has accumulated. Hamilton, Soley and Eichorn⁶⁶ have introduced the autoradiogram, by which they show, as would be expected, that hyperplastic thyroid tissue has the greatest ability to concentrate iodine. Perlman, Chaikoff and Morton⁶⁷ have studied iodine uptake by various tissues and find that thyroid tissue re-

tains over a hundred times as much as others. This is a confirmation of the observations by Hertz, Roberts, Means and Evans.⁶⁸ The authors conclude that the thyroid gland retains iodine selectively, whereas its escape from other tissues is by diffusion only. They also showed that thyroxine is rapidly formed in the thyroid glands of both rats and sheep, but that a larger portion of administered iodine is found in the form of diiodotyrosin than thyroxine. Leblond and Sue⁶⁹ have found that TSH augments the power of the thyroid gland to fix iodine. The ensemble of their results, they conclude, on animals hypophysectomized or treated with TSH shows that this hormone controls the metabolism of iodine in the thyroid. In view of the work of Chapman,^{33, 40} this statement may need some revision. In a later study, Mann, Leblond and Warren⁷⁰ gathered evidence which indicates that iodine does not exist as such in the noniodized gland of the dog. Inorganic iodine does not appear to be the major source of the iodine of diiodotyrosin. Therefore, the conversion of radioactive iodine into diiodotyrosin must take place at the cell membrane unless it arises elsewhere in the body and is secondarily fixed as such in the thyroid cells—a possibility that the authors consider unlikely. Diiodotyrosin appears to be the natural precursor of thyroxine. The radioactive iodine approach has even been applied to comparative physiology, Gorbman and Creaser⁷¹ having shown that iodine is specifically localized in the endostyle of lamprey larvae. This organ, therefore, must be a primordial thyroid gland.

The methods of determining the iodine levels of the blood have been improved to the point of great clinical usefulness. The information to be got is analogous to that yielded by the basal metabolic rates. Salter, Bassett and Sappington,⁷² for example, studying the relation of clinical symptoms, basal metabolic rate and blood iodine, found that in 71 cases in which the clinical impression of thyroid status—that is, hyperthyroid, euthyroid or hypothyroid—and the basal metabolic rate were in agreement, there was also a high degree of agreement between basal metabolic rate and the protein-bound iodine in the blood. In the 29 cases in which there was no such agreement, the blood iodine gave a better agreement with the clinical impression, and the authors therefore regard it as a better yardstick of thyroid function than the basal metabolic rate. It is, however, harder to do and more costly. Bassett, Coons and Salter,⁷³ studying the naturally occurring iodine fractions of the blood and their clinical behavior, divided these into T iodine (thyroxinelike), D iodine (diiodotyrosin-like), P iodine (protein bound) and

I iodine (inorganic) The ratio, T P, gave the following results in different states of thyroid function myxedema, 0.19, normal, 0.73, and hyperthyroidism, 0.76, 0.71 and 0.76 Thus, except in myxedema, in which little or no thyroxine circulates in the blood, the P fraction appears to be a practical and useful method for clinical investigation and routine diagnosis, because it affords at least a roughly quantitative measurement of the circulating thyroid hormone

The special ophthalmologic problems of Graves's disease hinted at in my previous report¹ have aroused much interest in the intervening years. Indeed, one might almost say that a new specialty of endocrinologic ophthalmology is a borning, and rightly so, for neither the endocrinologists nor the ophthalmologists seem to know much about this peculiar field. However, it is untrue to suggest that the subject is a new one. Marine³⁸ states that the experimental study of exophthalmos began as early as 1858 with the work of Muller,⁷⁴ and Gley,⁶ in 1910, reported that animals could develop exophthalmos following thyroidectomy. In discussion of Gley's paper, Poncet⁷⁰ remarked that the mechanism in Basedow's (Graves's) disease seems to result from a dysthyroidism amounting to a more or less severe poisoning. If then Gley had removed the entire thyroid-parathyroid apparatus, suggested Poncet, why might not there have been a vicarious exophthalmos producing action exerted by some other organ, perhaps the pituitary?⁷ Gley did not appear to value Poncet's suggestion very highly but it looks at present as though Poncet had made a very prophetic remark, and that Gley had missed the significance of his own observations.

The pathogenesis of exophthalmos has been studied both experimentally and clinically by many investigators, and it can be taken as well established as shown in 1932 by Loeb and Friedman⁷⁷ and in 1933 by Marine and Rosen,⁷⁸ that exophthalmos can be produced by the administration of anterior pituitary, and also that thyroidectomy enhances such action. Marine⁷⁹ further claims that both the adrenal glands and the gonads are involved in the endocrine hook up. Certainly, it appears that progressive exophthalmos is more easily produced experimentally in males, and although Graves's disease is more common in women, progressive or malignant exophthalmos is relatively more frequent in men. Other reports of experimental production of exophthalmos with anterior pituitary are numerous (Friedgood,⁸⁰ Smelser,⁸¹ Paulson⁸² and Aird⁸³). Also well established now is the fact that in human Graves's disease, exophthalmos may become aggravated and may take on a progressive course following thyroidectomy. Among recent papers on this subject are those of Daniels,⁸⁴ del

Castillo and Reforzo Membrives,⁸⁵ Jensen,⁸⁶ Means Hertz and Williams⁸¹ and Soley.⁸⁷

The pathology of progressive exophthalmos in Graves's disease seems to be established as one chiefly of swelling of the orbital muscles, with lymphoid infiltration, but also edema of the entire contents of the orbit (Dudgeon and Urquhart,⁸⁸ Moore,⁸⁹ Naffziger,⁹⁰ Duthie⁹¹ and Smelser⁹²). The sequence of events in its development has been reconstructed by Galli Mainini.⁹³

From the practical side, the important point is that there are certain patients with Graves's disease in whom thyroidectomy is contraindicated. They are to be recognized (Means, Hertz and Williams⁸¹ and Means⁸²) by the fact that their eye complaints and signs are more striking than their thyrotoxic ones, and that they make a superstandard response to iodine, often to minus levels of basal metabolic rate. Their thyrotoxicosis is usually easily handled by iodine alone, and when this is not sufficient, x-ray treatment to the thyroid may be used. For the eye condition, in which hyperfunction of the anterior pituitary—relative if not absolute—is probably a factor, thyroid may be given (on the theory that it depresses the pituitary), either alone or in combination with iodine. Humes⁹⁴ states that iodine and thyroid together have been used at the Mayo Clinic in cases of Graves's disease with severe ophthalmopathy and a low basal metabolic rate since 1922. Results are variable, but the treatment is worth trying, when it is insufficient, irradiation of the orbits or of the pituitary gland may be tried.

The use of thyroid for any purpose in the treatment of Graves's disease demands explanation. In addition to the indication mentioned above, Rienhoff⁹⁵ has used it for a different purpose, namely, to cause atrophy or prevent regeneration of the fragment left behind after subtotal thyroidectomy. For this purpose, he gives thyroid preoperatively to thyrotoxic patients and finds that no aggravation of symptoms results. In passing, we may note that Siley,⁹⁶ in 1896, claimed to have cured a case of Basedow's (Graves's) disease with thyroid tablets. Related to these observations of Rienhoff is that it also represents a suppression of thyroid activity by the administration of thyroid hormone, is the work of Farquharson and Squires,⁹⁷ in which it is shown that long-continued exhibition of thyroid to patients with so-called "nonmyxedematous hypometabolism" causes a depression in thyroid gland activity manifested by the fall of the basal metabolic rate on the omission of thyroid, to a lower level than the original one. The thyroid glands of these patients became indolent under the continued artificial supply of thyroid hormone, or perhaps their pituitary glands became indolent

and no longer stimulated their thyroid glands. Of course, the development of an antithyroid hormone during thyroid administration is another possible but, I believe, unlikely explanation of these results.

The question of liver involvement in thyrotoxicosis is always an important one. Haines, Magath and Power⁹⁸ find that the excretion of hippuric acid is reduced in a significant number of cases, an indication that the liver is often functionally disturbed. McIver and Winter⁹⁹ have shown experimentally that the administration of thyroxine increases the vulnerability of the liver to chloroform but, somewhat surprisingly, that this is not a result of glycogen depletion.

Of the treatment of Graves's disease in general, it is interesting that in the Thyroid Clinic of the Massachusetts General Hospital we have come full circle in a quarter century.¹⁰⁰ In the years 1919-1922, half the cases were treated by nonsurgical methods. In 1932-1935, surgery was employed in 95 per cent. In 1942, half surgical, half nonsurgical procedures are being employed. The nonsurgical cases include the special ophthalmopathic type in which we believe thyroidectomy contraindicated, and a variety of others treated successfully by iodine alone, radioactive iodine or x-ray.

In the field of myxedema, I should like to stress particularly the importance of distinguishing between the primary thyroid form and the pituitary form with secondary hypothyroidism (Castleman and Hertz,¹⁰¹ Means, Hertz and Lerman¹⁰² and Lerman and Stebbins¹⁰³). The practical reason is that the indications for treatment are different. Thyroid alone totally relieves the former; it is not alone sufficient in the latter, but must be supplemented by other endocrine agents and salt. The salt is used as a preventive to adrenocortical insufficiency, which may be induced by thyroid alone. Thompson and his co-workers¹⁰⁴ have shown that the administration of TSH has no effect in human myxedema. This is what one would expect. They¹⁰⁵ have also shown quantitatively the relative ineffectiveness of thyroxine by mouth. Talbot et al.¹⁰⁶ have demonstrated that the level of serum phosphatase of infants and children with untreated hypothyroidism is abnormally low. It is restored to normal by adequate thyroid therapy. The phosphatase level can be used as a measure of thyroid deficiency.

Angina pectoris, which appears in myxedema on treatment with thyroid, is well known and is one of the complications to guard against in the inauguration of substitution therapy. Mussio Fournier and Fischer¹⁰⁷ have shown that another type occurs while the patient is myxedematous and disappears on thyroid therapy.

What may be called a positively charming piece of research on hypothyroidism has been done by Richter,¹⁰⁸ who placed rats in cages and supplied them with rolls of paper from which they could tear off bits to make nests. The amount used in nest building was measured and found very constant: thyroidectomized rats used much more paper than normal ones. Recall the human being with myxedema who requires much more bed-clothing!

Of malignant disease of the thyroid, space permits me to say nothing. Perhaps, after all, this is not a thyroid but a cancer problem.

Of curiosities in the thyroid field, I may mention the report of an echinococcus cyst of the thyroid by Blum, Boquet and Hantcheff¹⁰⁹ and one of hemochromatosis of the thyroid gland by Graham and Mallory.¹¹⁰

In the field of surgery of the thyroid, there appears to be nothing radically new. The surgeon's point of view is well stated in a recent study by Albright and Clute.¹¹¹ It differs, of necessity, somewhat from that of the physician because the surgeon thinks in terms of operations, whereas the physician thinks in terms of patients. Certain patients will doubtless have to have portions of their thyroid glands removed for many years to come. Occasionally, they may require total thyroidectomy, and when such procedures are necessary, a high surgical skill is available. But removal is not always the best way to bring about restoration to health in the person with a diseased thyroid, nor are the results of removal always perfect. I shall close this report with the prophecy that surgery will be used less and less in this field as the endocrinology becomes better understood.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28421

PRESENTATION OF CASE

A sixty-nine-year-old physician was admitted because of severe chest pain.

Three years previously, the patient, who was known to have had hypertension for at least ten years, had suffered with occasional attacks of dyspnea accompanied by a feeling of faintness, which required admission to a hospital. After enforced rest, he recovered and was able to get about, enjoying only limited activity. However, in spite of this limitation of activity, he noticed occasional attacks of substernal oppression, particularly on exertion. During the next two years he again entered a hospital twice for brief periods of study and rest. He carried on very little practice during this time. Three months previously, the attacks of substernal discomfort became more severe and occurred more frequently, and two months later, he entered a community hospital. While there, he had more and more trouble of this same sort, even while resting in bed. During the fourth week of his hospital stay, after a good night and soon after waking, he was seized with a very severe anterior chest pain radiating down both arms, down his back and into both legs with great intensity. The leg pain was said to have been similar to that of sciatica. This attack continued more than twelve hours in spite of the repeated administration of Dilaudid.

Physical examination showed a well developed, obese man who was obviously acutely ill. He was slightly cyanotic and dyspneic. Breathing was irregular and of Cheyne-Stokes type. The examination of the heart revealed the maximum apical impulse 12 cm. to the left of the midsternal line in the sixth intercostal space. The retromammary dullness was not increased. The heart sounds were of mediocre quality. The rhythm was regular. The pulmonic second sound was sharp. No murmurs were audible. There was some increased filling of the neck veins. The radial pulse was thready, and the vessel wall was soft; no pulse deficit was noted. The lungs were normal. The abdomen was distended. No masses were felt, and no tenderness of the liver edge could be elic-

ited. There was a slight amount of pitting edema over both ankles. No pulse was felt in the vessels of the feet or in the groin. There was no clubbing of the fingers or toes.

The blood pressure was 150 systolic, 115 diastolic. A slight alternation of the pulse was noted when the blood pressure cuff was at this systolic pressure. The pulse rate was 110.

An electrocardiogram was said to have shown sinoauricular tachycardia. The cardiac rate was 120. The PR interval was 0.25 second. The T waves were low in Leads 1, 2 and 3 and of fair amplitude in Lead 4.

The patient did poorly, continued with the same picture of pain, shortness of breath and cyanosis and died four days later, in spite of supportive therapy in the form of oxygen and sedatives.

DIFFERENTIAL DIAGNOSIS

DR. FRANCIS R. DIEULAIDE. Although the recorded examination of the heart is not entirely clear so far as its size is concerned, I take it to mean enlargement, probably downward and outward, of moderate degree. The PR interval in the electrocardiogram was considerably more than it should have been. At the same time, there was no bradycardia, but a tachycardia. The patient was obese and was known to have had hypertension. These are general data of some importance.

To proceed at once to the final major episode, among the things one might consider is a large arterial embolus. That is suggested especially by the absence of pulsation in the feet and groin and perhaps might have fitted in with the attack of severe pain. But it seems very unlikely in this case. It offers no explanation of the preceding attack of pain or of the previous history of the patient. Furthermore there was no source for such an embolus. Large arterial emboli usually occur in cases of mitral valvular disease. This patient had no evidence of valvular disease, endocarditis or auricular fibrillation. It is true he had been in bed off and on. One might think of the possibility of his having a thrombus in a leg vein and an embolus from that, but to use that possibility one would have to suppose a "paradoxical embolus," which I cannot do.

The early story raises the question whether the patient had syphilitic aortitis. There is no report of a blood test for syphilis, which would not be decisive but which one would naturally like to have. Perhaps we might assume it had been done and was negative. There were no signs of aortic regurgitation, but we must remember, of course, that a patient may have a huge sacular aneurysm of the aorta without aortic regurgitation. There was no evidence of enlargement of the aorta on

physical examination, and we have no information about any x-ray picture of the chest. There was no physical sign of an aneurysm. On the other hand, one has to remember that an aneurysm at the back of the arch of the aorta or of the descending thoracic aorta would be extremely difficult to pick up on physical examination. Sometimes these are missed on x-ray examination. We know, in this connection, that the patient had hypertensive disease, which means that, if he had syphilitic arterial disease in addition, he had two diseases. I exclude syphilitic aortitis on the basis of the evidence that we have.

Then the question arises whether the patient had a dissecting aneurysm. It might, perhaps, be better if we had another name for that condition to separate it from saccular aneurysm, but the name seems to be fixed. The patient's age fits in satisfactorily enough. Most patients with dissecting aneurysm are between fifty and sixty, but I do not take the limits too seriously. The patient was known to have hypertension, which fits well with the diagnosis of dissecting aneurysm. The description of the major attack of pain is also compatible. We may guess that, soon after waking in the morning, the patient was not very active, so that there was no particular connection between the pain and activity, which is typical for the onset of dissection. Pain first occurred in the front of the chest and radiated down both arms. Radiation down the arms is much commoner with acute coronary occlusion than with dissecting aneurysm, but many cases of coronary occlusion have no radiation into the arms and a certain number of cases of dissecting aneurysm do have such radiation. The pain also went down the back and into both legs. I should take the radiation into the legs to be fairly strong evidence of dissection. The absence of pulsation in the groins and in the feet also fits in with dissection. We are not told the condition of the patient's legs and feet, except that they were pulseless. We do not know whether any neurologic changes or any limitation of motion existed.

DR. TRACY B. MALLORY: There were none.

DR. DIEUAIDE: It is an interesting fact that a group of patients with dissecting aneurysm, as well as patients with other aneurysms of the descending aorta, have various neurologic changes in the legs, which are very important diagnostically when they are present.

If we think the patient had a dissection I suppose the question might be raised whether he also had an old dissection, because we know that there are a few patients who have an almost silent dissection with formation of a second aorta and subsequent further dissection and rupture. We have

no particular reason to think that occurred in this patient, although I do not believe it is out of the question. The question might also be raised whether he is one of the few patients who have dissection with coarctation of the aorta. We have no good evidence of that. He had hypertension in his arms; we do not know the popliteal blood pressure.

Then we must, of course, consider the diagnosis that I mentioned first—coronary occlusion with myocardial infarction. The early part of the history very strongly suggests coronary sclerosis. These repeated attacks, rather severe in nature, are suggestive of coronary insufficiency. The major attack, following which the patient died, does not resemble the ordinary development of myocardial infarction. The disappearance of the pulsation in the legs has no particular relation to myocardial infarction, unless it were a later event, following embolism. The patient did not show the picture of shock following this accident, at least according to the data we have. The blood pressure was well maintained. In the case of an infarct followed shortly by death, the blood pressure usually falls markedly.

Then we come to the electrocardiogram, which is troublesome. It showed increased auriculoventricular conduction time (0.25 second). No statement is made regarding digitalis, which is an important omission.

DR. PAUL D. WHITE: That is an error. He had been fully digitalized because of the dyspnea—for some years, as a matter of fact.

DR. DIEUAIDE: He was digitalized, then, and had been regularly, so that although changes in the auriculoventricular conduction time are common in myocardial infarction, we ought to place this finding aside. It would be remarkable, however, to have increased auriculoventricular conduction time as the only electrocardiographic evidence of infarction.

DR. WHITE: May I correct my last statement? I find that, although he had had much digitalis in the past, he had had none within the last week or two. So there was not enough digitalis in his system to produce the delay in auriculoventricular conduction.

DR. DIEUAIDE: That makes this finding more important. Perhaps Dr. White would like to discuss it. Since digitalization is not the explanation, we must consider the other possibilities. The patient may have had a chronically prolonged conduction time as a part of arteriosclerotic heart disease. We do not know about that because we have no previous electrocardiogram. Myocardial infarction, however, seems to be a better explana-

tion At any rate, we cannot connect this finding with a dissecting aneurysm.

DR. WHITE: From my experience I should say the reverse, namely, that heart block, either auriculoventricular or intraventricular (bundle branch), is much more often evidence of chronic coronary heart disease than of an acute process. In most persons, heart block is discovered either accidentally by electrocardiograms or as a result of symptoms of faintness and not following a typical episode of acute myocardial infarction, whereas the great majority of patients who have perfectly classic attacks of acute myocardial infarction have no heart block at all or only for a few days, in the rare cases of posterior wall infarction. There are exceptions, but that is the rule.

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Dissecting aortic aneurysm
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Congestive failure.

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Myocardial infarction, old

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Dissecting aneurysm of aorta and great vessels of neck
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Arteriosclerosis coronary, moderate, and aortic, marked
Infarcts of kidneys, partial and complete

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an analysis of the deaths will clearly show how this can be lowered.

It must be borne in mind that the allocation of deaths was left entirely to the discretion of the investigator. An attempt was made to place each

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Transfusion	4
Suicide	2
Inverted uterus	2
Cerebral hemorrhage	2
Pernicious vomiting	2
Cause unknown	2
Shock	2
Abdominal pregnancy	1
Aneurysm	1
Chemical	1
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Psychosis	1
Sudden death	1
Anaphylaxis	1
Cancer of breast	1
Nonpuerperal	5
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Autopsy showed that the patient had rheumatic heart disease, pulmonary infarction and cerebral embolism. The patient died almost four weeks after delivery. The case was classed under "cardiac disease," because there was, in addition, a definite history of heart disease of many years' standing.

It is, in one sense, distinctly unfair to include cases of suicide in computing the maternal death rate. Pregnancy may have been a contributing factor in the mental unbalance associated with such fatalities, but the cases in no way represent obstetrical mismanagement. Furthermore, the case of aneurysm, although interesting in itself, was not a true maternal death.

Beginning with next week's issue of the *Journal*, the 48 cases of sepsis will be reviewed; and in subsequent issues, cases under the various other headings will be analyzed.

DEATH

HANDY—HARRY T. HANDY, M.D., of Scituate, died October 8. He was in his sixty-ninth year.

Born in Marion, Dr. Handy received his degree from Harvard Medical School in 1897. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, a brother and a sister.

MISCELLANY

NOTES

Eleven appointments to the teaching and research of the Harvard Medical School, effective during the present academic year, were recently announced as follows: assistant in ophthalmology, Fred S. Thorne, of Newton, M.D. Harvard '18; assistant in medicine, Jack D. Cole, of Brookline, M.D. Tufts '37; assistant in pediatrics, Edward L. Pratt, of Boston, M.D. Harvard '40; assistant in surgery, Arnold Starr, of Newton, M.D. Tufts '24; research fellow in anatomy, David L. Bassett, of Stanford University, California, M.D. Stanford '39; research fellow in medicine, Marshall Clinton, Jr., of Cambridge, Mass. Buffalo '40; research fellow in surgery, Mercier Falz of Westmount, Quebec, Canada, F.R.C.S. (C) Royal Canadian College of Surgery '31; Austin Teaching Fellow in Physiology, Aristides A. P. Leao, of Rio de Janeiro, B.Sc. M.A. Harvard '42; instructor in surgery, David D. Bar of Brookline, M.D. Tufts '23; assistant in bacteriology-immunology, Morris J. Pickett, of Boston, Ph.D. Stanford '42; research fellow in comparative pathology in tropical medicine, Henry D. Hoberman, of Bridgeport, Connecticut, Ph.D. Columbia '42. The appointments of Drs. Pickett and Hoberman are also effective in the Harvard School of Public Health.

CORRESPONDENCE

RELATION OF PERIPHERAL DISEASES TO PULMONARY FIBROSIS

To the Editor: In the past eighteen months, there has appeared in the *Journal* three papers of much greater significance than the implication of their titles. In the June 17, 1941, issue, Linenthal and Talkov reported 12 cases of pulmonary fibrosis in Raynaud's disease. In the September 17, 1942, issue, they reported two additional cases, whereas in the September 18, 1941, issue, Banks had a paper entitled, "Is there a Common Denominator in Scleroderma, Dermatomyositis, Disseminated Lupus Erythematosus, the Libman-Sacks Syndrome and Polymyositis Nodosa?" In the six cases reported by these three authors, Raynaud's disease, scleroderma and arthritis were associated with pulmonary fibrosis.

Ten years ago, I reported before the Boston Society of Psychiatry and Neurology a group of cases in which the conditions and Dupuytren's contracture were associated with pulmonary fibrosis and other pulmonary conditions. In the October, 1934, issue of the *Journal of Nervous and Mental Disease*, I reported twenty nine cases in which Raynaud's disease, scleroderma, Dupuytren's contracture, noninfectious arthritis and other peripheral conditions were associated with fibrosis and other pulmonary conditions, no prior description of this syndrome having been found in the literature.

Banks, Linenthal and Talkov, without having read my paper and, I believe, without obligation to any other authors, have now reported six cases exhibiting the syndrome, including complete laboratory data and complete pathological data. I say "almost complete pathological data" because I believe that, when the conditions in this syndrome appear clinically, the changes are present subclinically and may be found by the pathologist.

If this ten-year-old concept, that pulmonary fibrosis in Raynaud's disease, noninfectious arthritis, Dupuytren's

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The terminal episode was rupture of the outer layer of the aorta into the pericardium, with death from cardiac tamponade. The heart was markedly hypertrophied, weighing 800 grams. The coronary arteries showed moderate atheroma.

ies: No, because of the location. We never see fluid in that area. The heart is apparently normal.

MAN: The differential diagnosis here is at the types of mediastinal tumors. I discuss lesions arising outside the me-

chest to rest on the diaphragm, and it lodges posteriorly rather than anteriorly.

I do not believe this is an aneurysm, because no definite connection between the mass and the aorta was visualized. The presence of pulsations is not mentioned, although they are not absolutely neces-

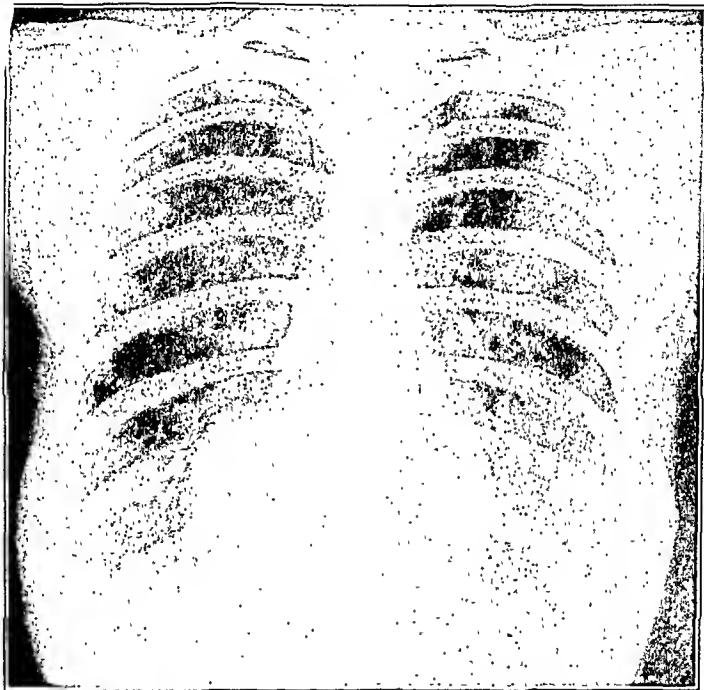


FIGURE 1.

diastinum that eventually lodge in the mediastinum, and second, lesions arising in the mediastinum itself.

One should consider diaphragmatic hernia. Only a very unusual one lodges in the right chest. One might suppose that the hernia went through the anterior attachment of the diaphragm. This type, however, is extremely rare, and I mention it only in passing.

Intrathoracic goiter has to be considered, but it must be of an extremely unusual type to fit this case. Intrathoracic goiters in this region are rare; most occur in the upper mediastinum. Certainly the shape of this tumor is unusual for intrathoracic goiter. Usually, it is a single round nodule and not a lobulated mass that plunges down into the

sary for diagnosis. Moreover, there is no history or physical findings of syphilis, and the Hinton test was negative. I am not at all concerned about aneurysm.

In considering the diagnosis of mediastinal tumor, one must first settle the question whether the mass is benign or malignant. I think we can state definitely that this mass is not a malignant tumor. The patient was symptomless, except for inconstant pain; there was no evidence of invasion of surrounding structures and organs, and there was no toxemia. Consequently, we can rule out a malignant type of tumor.

Although I doubt that I can make a better diagnosis than just benign mediastinal tumor, I must consider the several varieties. The description of

the tumor, the short duration of pain and the unknown duration of the tumor are consistent with dermoid, which also is the commonest statistically. On the other hand, several cases with similar findings that have been discussed at these meetings were found to have had either a neurofibroma, chondroma, lipoma or cyst. We saw one mediastinal tumor here a year ago that gave similar symptoms and had a similar appearance in the x-ray films, which the pathologist called hemangioma. One should mention thymoma as a possibility. It must have extended from its origin in the thymus down to this region. I have no way of confirming this diagnosis.

As Dr. Holmes said, it is unusual to find encapsulated fluid in this location, although the history of pleurisy a month before admission raises the question of fluid in the pleural space. Moreover, lobulation of the mass argues strongly against encapsulated fluid. Consequently, I shall not consider it further.

In conclusion, I believe this is a benign mediastinal tumor, either neurofibroma or dermoid.

DR. WILLIAM B. BREED: I wonder if enough stress has been laid on the fact that this whole episode was ushered in by an acute respiratory infection. That may be of some importance, and the mass may still be encapsulated pus. Perhaps this point should be stressed just a little more than it was in the discussion.

DR. LERNAN: Dr. Churchill has emphasized many times that the symptoms of these patients have no relation to the mediastinal tumor. I have been influenced by his opinion. Many patients come in with bizarre complaints, and a tumor is found incidentally. I think the onset of the respiratory infection served to focus attention on something in the chest.

DR. RALPH ADAMS: Did this mass move with swallowing?

DR. TRACY B. MALLORY: I do not believe so.

DR. EDWARD D. CHURCHILL: This is all a guessing game, for it is very difficult to arrive at any preoperative diagnosis except mediastinal tumor, benign or malignant. There are two or three additional diagnoses that occurred to me as I listened to the discussion. I should think of a hernia through one of the apertures of the diaphragm and should have advised a barium enema. There is another lesion that we have come to recognize particularly along the right border of the pericardium,—namely, a thin-walled cyst containing clear fluid. These cysts are comparable to the cystic hygromas that are found in the neck. Perhaps Dr. Mallory can say whether they are of lymphatic origin or of endothelial origin from adjacent serous cavities.

I wish Dr. Holmes would take a stand on the question whether this particular patient should have received a diagnostic dosage of radiation therapy to rule out lymphoma or another radio-sensitive tumor before operation.

DR. HOLMES: As a general rule, I think the diagnosis should be established, whenever possible, before we subject a patient to x-ray therapy. But it depends largely on the severity of the operative procedure planned. If it is to be a simple operation, probably x-ray therapy should not be given; on the other hand, if it is a dangerous operation, I should advise giving a small dose.

DR. CHURCHILL: Will you feel badly if some day I enucleate such a tumor and it turns out to be lymphosarcoma or lymphoma?

DR. HOLMES: No.

DR. CHURCHILL: Will you, Dr. Mallory?

DR. MALLORY: No. It might be good treatment. I think when an isolated tumor is resectable it is wise to remove it, because very long cures often follow the procedure.

CLINICAL DIAGNOSIS

Mediastinal tumor (? dermoid cyst, ? neurofibroma, ? lymphoblastoma).

DR. LERNAN'S DIAGNOSIS

Benign mediastinal tumor (neurofibroma or dermoid).

ANATOMICAL DIAGNOSIS

Pleuropericardial cyst.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient did turn out to have a cyst filled with perfectly clear fluid. The cyst has a fibrous wall with an occasional smooth muscle fiber in it, looking essentially like pleura. It is lined with a low cuboidal epithelium that occasionally seems multilayered, which is probably due to tangential sectioning; it seems likely that the epithelium lining was only a single layer thick. So far as the appearance of the cells is concerned, they could either be mesothelial, such as those that line the pleura, or endothelial, which one would find lining a lymphatic vessel. I do not believe I can answer Dr. Churchill's question. I have a little preference for the theory that this sac is made up of pleural or pericardial tissue than that it represents a cystic hemangiomatous tumor, such as a cystic the neck.

DR. HOLMES: Perhaps it is a change in shape had a thin wall

DR. MALLORY: Should this tumor perhaps have been needled before operation?

DR. CHURCHILL: I do not think so.

DR. MALLORY: If it had been, could you have made the diagnosis?

DR. CHURCHILL: Probably, but we should not have known what to do in the way of treatment. I do not believe it is without danger to put a needle in so close to the pericardium. There is always a possibility that one is dealing with an aneurysm of the auricle.

Dermoids are likely to be a bit higher on the right and a little closer to the lung root. When a tumor lies in the cardiophrenic angle, a simple cyst must be seriously considered.

DR. MALLORY: Sometimes, there is a rather unusually large amount of fat tissue in that loca-

tion. Does that ever cause clinical confusion in a case of this sort?

DR. CHURCHILL: I do not recall having been misled by a fat pad.

DR. ALLEN G. BRAILEY: The patient would have been perfectly well if left alone?

DR. CHURCHILL: I think she would have.

DR. MALLORY: We have no idea of the rate with which these cysts grow. It is quite doubtful that this had anything to do with the symptoms.

DR. CHURCHILL: I also think that it is very doubtful. One must remember, however, that the presence of an x-ray shadow of this type is sufficient reason for employment rejection by many large industrial plants and, of course, by the armed forces. She can now join the WAACs or WAVES.

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MATERIAL for early publication should be received not later than noon on Friday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

AN ELOQUENT SERMON

The number of physicians on extended active duty and the figures on the 1942 quotas, as of September 1, are now available from the Procurement and Assignment Service. The latter furnish interesting and disturbing data, particularly concerning some of the New England states. The state providing the lowest percentage of its quota of physicians for 1942 is Nevada, which has obtained but 56 per cent. The second lowest is Illinois, in which the figure is 63 per cent. The next two lowest are Connecticut and New York, each having supplied but 64 per cent of their quotas. For Massachusetts, the figure is 67 per cent; for New Hampshire, 79 per cent;

for Vermont, 82 per cent; for Rhode Island, 84 per cent; and for Maine, 99 per cent.

For a community spoken of as the "Cradle of Liberty," Massachusetts hardly shows to advantage in this picture when compared with such states as New Mexico with 203 per cent of its total quota, Louisiana, with 196 per cent, Alabama, with 179 per cent, South Carolina, with 160 per cent, Kentucky, with 159 per cent, and North Carolina, with 151 per cent. Twenty-six states in the Union have supplied above 100 per cent of their quotas. When one realizes that Massachusetts stands fifth from the bottom, only four other states, Nevada, Illinois, Connecticut and New York, having lower percentages, then it can be said that these figures preach an eloquent sermon.

A SEMICENTENNIAL

It is occasionally valuable to stop in the course of one's daily rounds and survey the activities of one's fellow workers. The opportunity usually arises in relation to an anniversary, a birthday or the completion of a long period of service. Such an event will be celebrated on Friday, October 23, at the Boston Medical Library, for on that date Mr. James F. Ballard, the director, will have completed a service of fifty years as a valued employee of that institution.

Beginning in 1892, as a boy helping in the stacks, Mr. Ballard has worked his way up to the directorship of the library and has made a name for himself in the front rank of medical librarians. This position has been recognized by his election to the presidency of the Medical Library Association and to other offices. He is widely known for his classification of medical books, which is used in almost every medical library in this country. In the past, he has been consulted by the Rockefeller Foundation and its General Education Board for advice in establishing medical libraries in this country and abroad. There are few men living who know more about medical books and their accession, classification and care. His knowledge of medical periodicals, moreover, is extensive.

It should be pointed out that, in addition to his work as a medical librarian, he has been for many years a substantial citizen of the Town of Milton, has sent three of his children through college and has two sons now serving in the armed forces.

This creditable career is largely the result of his own efforts, for his preliminary schooling was scant and knowledge came to him largely through continued application and long hours of hard work. His nights, Sundays and holidays, which for many people are times of relaxation, have been freely and almost continuously given to the Boston Medical Library. Rarely would one not find him at work in the evening or on Sunday afternoon, particularly during the last twenty five years, when he has had executive responsibility.

It is of interest, moreover, that he chose as his hobby one of the most difficult branches of medical literature, namely, incunabula or books printed in the fifteenth century. Here he had to acquire a working knowledge of Latin and a deep appreciation of these books and their significance, as well as a considerable technical knowledge regarding their classification, for the printer, place of publication and author are often unknown. There are, in addition, many details to be learned about the type used, the paper, the dating of the publication and the relation of the printed book to the same material in manuscript form circulated before the discovery of printing. All these have been Mr. Ballard's particular interest in the last two decades, and the library has turned to him for a new catalogue of its renaissance and medieval manuscripts and its incunabula, which is now in the course of publication.

Few individuals have the opportunity of serving one organization for half a century. It is even rarer to have the service so genuine and efficient as that given by Mr. Ballard to the Boston Medical Library. The *Journal* therefore takes great pleasure in extending to him heartiest congratulations on this semicentennial anniversary and wishes him good health in the future so that he may continue his work, the thing nearest his heart.

MEDICAL EPONYM

ROVSING'S SIGN

Dr Thorkild Rovsing (1862-1927), director of the Surgical Clinic at the University in Copenhagen, described "Indirektes Hervorrufen des typischen Schmerzes an McBurney's Punkt [Indirect Elicitation of Typical Pain over McBurney's Point]," in the *Zentralblatt für Chirurgie* (34: 1257-1259, 1907). Being unable satisfactorily to examine in the usual way two patients whom he suspected of having appendicitis, he was able to bring out the typical pain by this maneuver. A portion of the translation follows:

Both patients showed such unusual sensitiveness to palpation that a careful examination of the region of McBurney's point seemed not only impossible but inadvisable. It occurred to me that the typical pain might possibly be elicited by pressure on the descending colon, in the left iliac fossa. I laid my left hand flat on the abdomen and with the right hand forced its fingers down against the colon, compressing it. The hand was then allowed to glide upward toward the sigmoid flexure.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

The five year study of the maternal mortality in Massachusetts, conducted by the Section of Obstetrics and Gynecology, ended with the deaths occurring during the year 1941. Two hundred and forty seven deaths were listed by the Massachusetts Department of Public Health for investigation, and of these, 5 were found, after investigation, to have no relation to pregnancy. Although these are included in the tabulation of the causes of maternal deaths (Table I), the cases will not be reviewed. An example of such a case is as follows:

Following the death of this patient, autopsy proved that pregnancy did not exist. The patient died of septicemia, peritonitis and parametrial abscess. One pregnancy preceded this fatality by eleven months, but there was no subsequent history of abortion, nor did the autopsy reveal any uterine change characteristic of pregnancy.

The death rate, 29 per 1000 living births, was practically identical with that for 1940, which was 28 per cent. Although that is a creditable figure,

an analysis of the deaths will clearly show how this can be lowered.

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MISCELLANY

NOTES

Eleven appointments to the teaching and research staff at the Harvard Medical School, effective during the present academic year, were recently announced as follows: assistant in ophthalmology, Fred S. Thorne, of Newtonville, M.D. Harvard '18; assistant in medicine, Jack D. Cohen, of Brookline, M.D. Tufts '37; assistant in pediatrics, Edward L. Pratt, of Boston, M.D. Harvard '40; assistant in surgery, Arnold Starr, of Newton, M.D. Tufts '28; research fellow in anatomy, David L. Bassett, of Stanford University, California, M.D. Stanford '39; research fellow in medicine, Marshall Clinton, Jr., of Cambridge, Md. Buffalo '40; research fellow in surgery, Mercier Fauteux, of Westmount, Quebec, Canada, F.R.C.S. (C) Royal Canadian College of Surgery '31; Austin Teaching Fellow in Physiology, Aristides A. P. Leao, of Rio de Janeiro, Brazil, M.A. Harvard '42; instructor in surgery, David D. Berlin, of Brookline, M.D. Tufts '23; assistant in bacteriology and immunology, Morris J. Pickett, of Boston, Ph.D. Stanford '42; research fellow in comparative pathology and tropical medicine, Henry D. Hoberman, of Bridgeport, Connecticut, Ph.D. Columbia '42. The appointments of Drs. Pickett and Hoberman are also effective in the Harvard School of Public Health.

CORRESPONDENCE

RELATION OF PERIPHERAL DISEASES TO PULMONARY FIBROSIS

To the Editor: In the past eighteen months, there have appeared in the *Journal* three papers of much greater significance than the implication of their titles. In the April 17, 1941, issue, Linenthal and Talkov reported three cases of pulmonary fibrosis in Raynaud's disease, and in the September 17, 1942, issue, they reported two additional cases, whereas in the September 18, 1941, issue, Banks had a paper entitled, "Is there a Common Denominator in Scleroderma, Dermatomyositis, Disseminated Lupus Erythematosus, the Libman-Sacks Syndrome and Polyarteritis Nodosa?" In the six cases reported by these three authors, Raynaud's disease, scleroderma and arthritic conditions were associated with pulmonary fibrosis.

Ten years ago, I reported before the Boston Society of Psychiatry and Neurology a group of cases in which these conditions and Dupuytren's contracture were associated with pulmonary fibrosis and other pulmonary conditions, and in the October, 1934, issue of the *Journal of Nervous and Mental Disease*, I reported twenty-nine cases in which Raynaud's disease, scleroderma, Dupuytren's contracture, noninfectious arthritis and other peripheral conditions were associated with fibrosis and other pulmonary conditions, no prior description of this syndrome having been found in the literature.

Banks, Linenthal and Talkov, without having read this paper and, I believe, without obligation to any other authors, have now reported six cases exhibiting this syndrome, including complete laboratory data and almost complete pathological data. I say "almost complete pathological data" because I believe that, when one of the conditions in this syndrome appears clinically, the others are present subclinically and may be found by the pathologist.

If this ten-year-old concept, that pulmonary fibrosis, Raynaud's disease, noninfectious arthritis, Dupuytren's

contracture, sclerodema and some other conditions are not clinical entities but parts of a syndrome, is once accepted, then progress in the study of every one of these conditions should be accelerated

Hale Powers, M.D.

203 Grove Street
Wellesley, Massachusetts

BOOK REVIEWS

The 1941 Year Book of Industrial and Orthopedic Surgery. Edited by Charles F. Painter, M.D. 12", cloth, 432 pp., with 353 illustrations. Chicago: The Year Book Publishers, Incorporated, 1941. \$3.00

Dr Painter is to be congratulated on the clear and concise manner in which he has summarized the contributions to orthopedic surgery that have been published during the past year. Each article has a new idea and a different approach to treatment. A larger section has been written on industrial medicine in an attempt to keep pace with this important branch of medical practice. There are numerous excellent illustrations. The selection and arrangement of the material are good. Although no two persons compiling a year book on orthopedic surgery would make identical selections of articles, there are few who would criticize the selections Dr Painter has made. This little book should be on the reading list of all industrial and orthopedic surgeons.

Rabies. By Leslie T. Webster, M.D. 8", cloth, 168 pp., with 8 illustrations and 22 tables. New York: The Macmillan Company, 1942. \$1.75.

In much of the literature on rabies, the lines between scientific fact and speculation have not been clearly drawn, and many of the articles are not easily accessible. This book is a compilation of existing literature and attempts to furnish sound data to those who would otherwise have difficulty in obtaining it. The first part of the book discusses the diagnosis of the disease, and the second covers its prevention, citing controversial results. It is stated, contrary to popular opinion, that 'there is no definite evidence that vaccine treatment, following exposure to rabies, confers any striking protection against the disease and that investigations of the efficacy of vaccine treatment should be continued from all angles'. The author states emphatically, however, that persons exposed to rabies should be given vaccine treatment with confidence that then there is small likelihood of development of the disease.

This book should be of great value to physicians, veterinarians, public health officials and research workers but, because of its technical nature, is not suitable for laymen.

The 1941 Year Book of Pathology and Immunology. Edited by Howard T. Karsner, M.D. *Immunology*. Edited by Sanford B. Hooker, M.D. 12", cloth, 623 pp., with 136 illustrations. Chicago: The Year Book Publishers, 1941. \$3.00

This book gives well selected reviews of the developments in pathology and immunology during 1941. However, comparing the abstracted articles with such a complete list as that given in the *Index Medicus*, one finds that it deals almost entirely with papers in English,

owing to abnormal wartime conditions, which limit the availability of almost all scientific journals issued abroad.

The twelve chapters on pathology, edited by the experienced and dynamic director of the Institute of Pathology of Western Reserve University, take up 349 pages and review general pathology and the pathology of tumors, of the cardiovascular, hematopoietic, respiratory, urinary and nervous systems, of the alimentary tract, of the male and female genitalia, of the organs of locomotion and of the glands of internal secretion. In this section, there are 129 illustrations, all reproduced from the articles abstracted, most of them are photographs showing histologic features of lesions, which are of great value to the reader. Among the large amount of information yielded by hundreds of analyses that are presented to the reader, the following are of particular interest: a review prepared at the invitation of the editor by Virgil A. Moon on the pathologic changes underlying the development of shock, a summary given by Eben J. Carey of his contributions to knowledge of the function of striated muscles, an abstract of studies on the bicuspidal semilunar valves, furnished by Simon Kalesky, an interesting review prepared by Aldo Luisada on favism, and data from Page on the new aspects of the nature of chemical changes occurring in arteriosclerosis. The interpretation of the analyses is helped by timely observations from the editor. A few papers, such as the one of Esmond R. Long entitled 'Constitution and Related Factors in Resistance to Tuberculosis' and three others, dealing respectively with transmission of susceptibility to cancer, the identity of inhibitor and antibody in virus-induced rabbit papillomas and the union in vitro of the papilloma virus and its antibody, are included in the section covering the pathology of tumors although their subjects, being of immunologic nature, ought to be included in the section on immunity to tumors.

The second part starts with a tribute to Hans Zinsser by his successor, J. Howard Mueller. Zinsser, who served Harvard, Columbia and Stanford universities as bacteriologist and immunologist for more than thirty-five years, had been properly regarded, for more than a quarter of a century throughout the world, as the academic personification of immunology applied to the study of infectious diseases. The chief attraction in this part of the book is found in the chapter on blood groups, where the recent advances in blood transfusion, inaugurated by Landsteiner and Wiener's discovery of the Rh factor and its relation to erythroblastosis foetalis, are authoritatively discussed by Wiener himself and by Philip Levine. The contributions in the various fields of immunity are divided into chapters dealing with immunity to bacterial diseases, immunity to viral diseases, immunity to diseases due to protozoa, fungi and higher parasites, immunity to tumors, chemotherapy, anaphylaxis and allergy, blood groups, immunochimistry, bacteriology and bacterial nutrition, and techniques and miscellaneous topics. In the first chapter, the influence of war is reflected in the prevalence of papers dealing with tetanus, although the flow of publications on immunity concerning diptheria and pneumococcal infections and so forth is not lowered. In the chapter on viral infections, in which an introductory article by Thomas M. Rivers gives a résumé of current developments in this field and the growing importance of vaccines for prevention, the recent research work on bacteriophage, cephalomyelitis, choriomeningitis, poliomyelitis and so forth is ably reviewed, however, owing to the war and to the interest in Horsfall's vaccine, papers dealing with influenza virus prevail. The chapter on the immunology of para-

sitic diseases supplies additional information to that included in Culbertson's book on immunity against animal parasites. Immunity to tumors supplements the section on their pathology edited by Karsner, whereas the chapter on chemotherapy merely supplements the subject, which is more extensively reviewed in other volumes of the series, its inclusion being justified by a sort of synergism between chemotherapeutic agents and antibodies in pneumonia and by the remarkable contributions supplied to this field of gramicidin and tyrothricin, the bactericidal fractions prepared from René J. Dubos's aerobic, sporulating soil bacillus. Those especially interested in the fields of anaphylaxis, allergy and immunochemistry in the realm of antigens and antibodies will find these sections particularly instructive on account of the critical remarks and suggestions, which are presented as a comment of the editor to some of the papers reviewed. A few illustrations and a table showing the clinically important cutaneous tests, which have been taken from an article of Charles A. Janeway, also give useful information and witness the ability of the editor to convey knowledge to the reader. When details on the methods used are essential, as in Landsteiner's and Di Somma's sensitization of animals with simple chemical compounds or in Heidelberger's quantitative chemical studies on complement, the editor reproduces them thoroughly from the original articles. An up-to-date report on the developing egg as a culture medium heads the reviews on bacterial nutrition, and a description of the electron microscope begins the last chapter, which is devoted to techniques and miscellaneous topics.

A comprehensive index to subjects and authors, covering both pathology and immunology, supplies a valuable guide to this book.

Biological Symposia. A series of volumes devoted to current symposia in the field of biology. Edited by Jaques Cattell. Vol. V. *Comparative biochemistry: intermediate metabolism of fats, carbohydrate metabolism, biochemistry of choline.* Edited by Howard B. Lewis, Ph.D. 8°, cloth, 247 pp., with 31 tables, 20 figures and 2 plates. Lancaster, Pennsylvania: The Jaques Cattell Press, 1941. \$3.00.

This is the latest of a series in biology published by the Jaques Cattell Press, and comprises the four symposiums arranged by the Council of the American Society of Biological Chemists for the April, 1941, meeting of the Federation of American Societies for Experimental Biology. It is thus well planned and authoritative. The contributors include such eminent investigators as Samuel Soskin, H. E. Longenecker, C. F. Cori, Otto Meyerhof and Vincent du Vigneaud. There are fifteen papers in all. Each is limited to ten to fifteen pages, which makes assimilation of the subject matter easy.

The first symposium, on comparative biochemistry, seeks to show some of the phases of modern biochemistry as they apply to plants and to animals and birds. An interesting question raised in plant biochemistry is the significance of the alkaloids, which may represent unexpected end products of the plant's nitrogen metabolism. The importance of niacin (nicotinic acid), choline and the betaines in plants, as well as in man, is discussed. In a paper on end products of nitrogen metabolism in animals, a comparative study is made of mechanisms of conjugation of nitrogenous products, and of variations in uric acid and purine metabolism. A third paper, on the merging of growth factors and vitamins, points out that choline is an essential growth factor for the pneumococcus, and nicotinic acid for *Staphylococcus aureus*.

In the symposium on the intermediate metabolism of fats, Soskin and Levine state that ketone bodies are formed because of faulty carbohydrate oxidation, but occur normally and independently of such oxidation. The peripheral tissues of the diabetic patient dispose of ketone bodies as fast as those of the normal person, and when ketone bodies appear in excess, it is due only to accelerated production of these substances in the liver. Thus the "ketogenic antiketogenic ratios," as formerly used, are meaningless.

One of the most interesting papers in the book is that of Longenecker on the formation of animal body fat. It has recently been shown, by "tagging" molecules with deuterium in place of hydrogen atoms, that the depot fat, instead of being laid down only in periods of excess food intake, is constantly in a state of flux, although its amount may not change. The conversion of fat to carbohydrate has also been traced by the use of deuterium. It was shown experimentally by Longenecker that protein can be converted to fat in the animal body. In these conversions between carbohydrate, protein and fat, certain members of the vitamin B complex are essential.

The symposium on carbohydrate metabolism comprises four papers, all dealing with enzyme reactions, the oxidation catalysts, including the flavoproteins and cytochromes, the process of aerobic phosphorylation of glycogen, by which the energy from oxidations is made available to the cell for its use; the "oxidoreductions," or anaerobic molecular rearrangements; and the oxidation of pyruvic acid by the "citric acid cycle," essential in intermediate carbohydrate metabolism.

The fourth symposium, on the biochemistry of choline, is of great interest. Choline has recently been shown to prevent or cure fatty livers in depancreatized dogs or in rats fed a high-fat diet. This property of choline is known as its "lipotropic effect." Choline deficiency in the diet causes an acute hemorrhagic degeneration in the kidneys of rats. In the body, choline stimulates the formation of phospholipids, permits the production of acetylcholine and, most significant, supplies "labile" methyl groups that the body cannot synthesize but must have for numerous methylations. One paper discusses the enzyme, cholinesterase, which destroys acetylcholine. In the final paper, du Vigneaud discusses the interrelations between choline and other methylated compounds. He and his co-workers, by the use of deuterium in methyl groups, were able to show that choline is definitely an essential dietary factor and that its methyl groups are concerned with methionine and sulfur metabolism, with creatine metabolism and with fat metabolism.

Altogether, this most stimulating collection of papers is highly recommended.

Psychosurgery: Intelligence, emotion and social behavior following prefrontal lobotomy for mental disorders. By Walter Freeman, M.D., Ph.D., and James W. Watts, M.D. With special psychometric and personality profile studies by Thelma Hunt, M.D., Ph.D. 4°, cloth, 337 pp., with 81 illustrations. Springfield, Illinois: Charles C. Thomas, 1942. \$4.00.

Since 1900, there have been three important new approaches toward solving the problem of mental disease. The first is psychoanalysis, which has brought many new ideas to medicine, especially regarding emotional patterns. The second is shock therapy, employing insulin, Metrazol and other chemical and physical means of altering or influencing the course of mental disease. The third

and newest of these methods involves operation on the brain itself—prefrontal lobotomy

This new book, the first of its kind, describes the intelligence, emotions and social behavior of patients who have undergone prefrontal lobotomy for mental disorders. The work has been carefully planned and executed and leaves little to be desired in terms of complete and conscientious reporting. The surgeon will find the book interesting, just as he might have found Dr. Cushing's book on meningiomas of interest. In fact, the general outline of case study employed by Cushing has been followed by the authors. The psychiatrist will find the reports valuable in view of the alterations in personality following operation.

This is an unusual book in that it combines three important kinds of observation in one document. It includes the clinical history, with emphasis on the mental disorder, and gives a detailed account of the surgical procedure that was followed and of the follow up reports, which are interesting and unique. In some cases, neuropathologic reports were available, and in the more successful cases detailed psychometric studies were utilized to measure the changes and improvement shown by the patient.

The authors have been very modest in reporting their results. They are keenly aware of the limitations and the experimental aspects of their studies. At the same time, they report enough substantial data to support interesting and encouraging conclusions. Until now, physicians have had to ask, Does cutting into the brain improve insanity? The answer contained in this book is, In some cases, improvement from certain psychiatric disorders has followed prefrontal lobotomy. The book is quite technical, but each physician should read it for himself to obtain his own impression. There are a few minor defects, which can be discounted in view of the great historical importance of the book.

Many neurosurgeons at present are extremely conservative in their approach to mental disorder. This book clearly indicates the type of patient for whom the operation may be suitable, and it describes with adequate clarity the technique and general management of the case.

In some quarters, the entire process of operating on the brain for mental disorder has been frowned on, since it has been regarded as too dangerous and too radical. From a study of the cases in this book, however, one gains the impression that the actual operation is not so radical as it sounds.

The book will probably do much to focus the attention of neurosurgeons and general surgeons on this problem and to stimulate their interest in the subject and their criticism of the method.

From Cretin to Genius By Serge Voronoff 8°, cloth, 281 pp. New York: Alliance Book Corporation, 1941 \$2.75

The author analyzes, in a philosophical vein, genius, the soul, the mind, the creative process and similar topics. He uses a wealth of observations on poets, writers, composers, artists and scientists, with considerable historical accuracy. When he comes to theorize about his material, however, he falls far short of scientific standards. He concludes, for example, that the conscious ego occupies the superficial layer of the brain, and the subconscious the lower layers. It is from these lower layers that come the profoundest thoughts of philosophers, the loftiest flights of poets, the proudest creations of artists, the noblest discoveries and inventions of scientists. Again, when discussing the electroencephalogram, he writes: "Scanning the chart, we can tell whether the thought was joyous or sad, whether

the feeling experienced was happy or painful. For the electric waves change according to the character of each thought and each feeling." These are far cries from the known physiologic facts, and based on such premises, the author's arguments are highly speculative and often unwarranted.

Preeclamptic and Eclamptic Toxemia of Pregnancy By Lewis Dexter, M.D., and the late Soma Weiss, M.D. In collaboration with Florence W. Haynes, Herbert S. Sise and James V. Warren 8°, cloth, 415 pp., with 47 illustrations. Boston: Little, Brown and Company, 1941 \$5.00

This monograph approaches the subject from the standpoint of the internist and the research worker, rather than from that of the obstetrician. The obstetric point of view, however, is not lost sight of, since the practical application of the research carried out is stressed throughout the book. The purpose of the monograph, as stated by the authors, is twofold: to describe their experiences and interpret their findings, and to analyze the literature in the light of their studies. A timely, well-sifted bibliography is appended at the end of each chapter, making important references readily available.

Consideration is given to the nature and significance of generalized edema in normal pregnancy and in toxemia of pregnancy. The authors believe that the etiology of generalized edema cannot be explained by the well recognized mechanical causes of edema formation, including hydrostatic pressure in the capillaries, increased capillary permeability to protein and hypoproteinemia. Nor do they regard it as due to cardiac failure, anemia, vitamin B₁ deficiency, myxedema or excessive ingestion of sodium salts. By exclusion, they suspect a primary, humoral etiology. The relation of the pressor fraction of the posterior pituitary gland to the hypertension of toxemia of pregnancy is fully discussed. Under the conditions of their experiments, Pitressin did not produce permanent hypertension when administered in both large and small repeated doses. No significant histologic changes were observed in the animals under the experimental conditions employed. So far as could be determined by the methods of extraction now in use, the pressor substance, renin, is not concentrated in the placentas of women with hypertension during pregnancy. A chapter is devoted to the arterial blood pressures of newborn babies of normal and hypertensive mothers, no significant difference in the blood pressures was found to exist. Hormones have not induced a syndrome strictly comparable to human toxemia in animals, nor does toxemia occur in them spontaneously. From their studies, the writers postulate that the improvement in blood pressure, albuminuria and edema that occurs promptly in toxemic patients following delivery is due to the removal of the placenta rather than to the removal of the fetus or to the relief of pressure on neighboring structures by the enlarged uterus.

One hundred and fifty-nine pages are devoted to the pre-eclamptic and eclamptic toxemias of pregnancy (arterial hypertension in pregnancy and the hypertensive toxemia of pregnancy). Eighty cases showing hypertension previous to the pregnancy studies were exhaustively investigated. The illustrations of the pathologic processes studied are clear and well chosen. An interesting diagram representing the factors involved in toxemia and post-toxemia is presented. Two types of hypertension in pregnancy have been differentiated—the pre-pregnant hypertension, uninfluenced by pregnancy, and hypertensive toxemia of preg-

nancy, which may occur in patients with or without pre-pregnant hypertension.

The chapter on treatment starts with the earlier methods, and considers all advances made in the management of this disorder. The authors advise a middle course, stressing individualization of the patient. Methods that have been found valuable are summarized under "Present-Day Treatment." Diekmann's and Irving's treatments are completely outlined and cover what is accepted as satisfactory management. Prenatal care is emphasized as an essential part of the care of these patients.

The text is interesting to read, and the illustrations are excellent. This monograph will benefit not only the student of the toxemias of pregnancy and the research worker but also the general practitioner and the clinical obstetrician.

Immunology. By Noble P. Sherwood, Ph.D., M.D. Second edition. 8°, cloth, 639 pp., with 27 illustrations and 7 color plates. St. Louis: The C. V. Mosby Company, 1941. \$6.50.

This is the second edition of an introductory textbook intended for the use of medical students and others interested in immunology and serology. It contains much that should interest the clinician.

It is clearly and simply written. The author is careful to define terms that may be unfamiliar to some of his readers. The material has been rearranged so that it may be outlined more readily, and two new chapters, one on the reticuloendothelial system and the other on serum reactions, have been added. A brief introduction to colloid chemistry has been retained. Most of the references, which are unusually numerous and well chosen, have been brought up to date. The index is adequate, typographical and grammatical errors are few, and the diagrams and illustrations, several in color, are helpful.

The author tends to cite in detail the conclusions of individual research workers, which sometimes leads to unnecessary duplication. At the ends of many chapters, however, he presents well-integrated summaries and his own interpretations of the often conflicting experimental data. The historical aspects of the various subjects are briefly but adequately covered. The chapters on antigens, antibodies and specificity as applied to the laboratory diagnosis of the common infectious diseases, although a little more up to date than they were in the first edition, are not so authoritatively covered as they are in certain other texts. The chapters on complement fixation and other serologic technics, however, are especially well done.

Directory of Medical Specialists Certified by American Boards, 1942. 8°, cloth, 2495 pp. New York: published for the Advisory Board for Medical Specialists by Columbia University Press, 1942. \$7.00.

This second edition of the *Directory of Medical Specialists* contains over 18,000 names of doctors certified by the fifteen American boards. Since the publication of the first edition in 1939, over four thousand physicians have successfully taken board examinations, and their names are to be found in the new edition. New information, especially concerning the graduate and postgraduate education of the diplomates, has been added. The directory has been increased in size by over nine hundred pages. Three new boards, on anesthesiology, plastic surgery and neurologic surgery, have been established since 1939, and their membership is included in the directory.

The indexing is seriously defective, since it omits the page on which the entry to the individual person is made.

This omission causes unnecessary delay when one desires information on a particular person. One must first look for the name in the index, where the address and certifying board are found. This is a poor beginning, for it is necessary to look in succession for the special board, the state and the city or town, which are arranged alphabetically. All this searching would be obviated if the index noted the page in the volume where the name is listed. It is hoped that the editors will make this change in the next edition.

The work is extremely bulky, but is of inestimable value as a book of reference.

Diseases of the Nervous System, Described for Practitioners and Students. By F. M. R. Walshe, O.B.E., M.D., D.Sc., F.R.C.P. (Lond.), D.Sc. (hon.). Second edition. 8°, cloth, 35 pp., with 32 illustrations. Baltimore: The Williams and Wilkins Company, 1941. \$4.50.

The fact that a second edition of this book was called for within two years is a tribute to its worth. The volume is a kind of personal report from a distinguished British neurologist, giving a summary of his experiences in a difficult field of medicine. Because of the outstanding position held by the author and his ability to write clearly and comprehensively, the book may safely be put in the hands of medical students and practitioners.

Readers should be warned, however, that they may find some personal reactions, especially to treatment, not widely held in this country. Such a statement as "tryparsamide is used in the post-pyrexial treatment of dementia paralytica" is correct but the drug is used extensively and favorable in other ways. Also, the statement that "the so-called Bulgarian belladonna treatment has no advantages over other measures" in the treatment of post-encephalitis Parkinsonism is too dogmatic for a controversial issue. Some drugs are referred to by their British trade names, unfamiliar to many American physicians. The Bragg-Paul type respirator is recommended, but in this country the Drinker box type is almost routinely used. With these points in mind, however, an American reader will find little difficulty in gaining a knowledge of clinical neurology from this book, which reflects the sound views of a leader in the field.

Your Teeth: Their past, present and probable future. By Peter J. Brekhus, D.D.S. With a foreword by Irvine McQuarrie, Ph.D., M.D. 8°, cloth, 255 pp., with 20 illustrations, 31 plates and 7 tables. Minneapolis: The University of Minnesota Press, 1941. \$2.50.

This volume represents a compilation of facts and theories pertaining to dental health. The book is not intended as a text for the dental practitioner or student, but fills a gap as an informative source, useful to the layman as well as to the dentist.

Excellent chapters on the biologic and anthropologic factors concerning the development and loss of teeth are presented. A discussion on the causes of caries and pyorrhea, with a voluminous bibliography, is especially valuable.

A program for prevention of caries, with special reference to the care of children's teeth, is constructive and worthy of consideration in mapping out a nationwide program for the control of dental caries, which is so widespread in present civilization.

The author has approached the subject from a long experience in both clinical and scientific studies, with a broad vision of the future of dentistry and suggestions for further investigative studies.

(Notices on page x)

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AUDIOMETRY IN GENERAL PRACTICE

WERNER MUELLER, M.D.*

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"THE proof of the deafness is in the hearing," to paraphrase an old adage. Essential as the physical examination of the ear is, it gives no accurate clue to the efficiency of that ear. One is often amazed at the acuity of an ear showing the effects of severe mechanical damage, where is a person presenting anatomically perfect eardrums may be profoundly deaf. If one adds to this the fact that in by far the greatest number of cases the onset of the deafness is very insidious, one may say that audiometry is of paramount value in the detection of deafness. It is the purpose of this paper to describe some of the various means and methods of testing hearing, especially those that should be incorporated in the daily routine of medical practice.

For the past several years, two types of electric audiometer have been extensively used by otologists, hospitals, laboratories and schools in the detection and the measurement of deafness. The so-called "pure tone" audiometers produce musical tones of variable pitch and intensity by means of electric oscillators. With their aid, the hearing acuity of an ear can be charted in the form of a curve. Their use requires a good deal of practice and application, especially since, in spite of their much vaunted "scientific accuracy," they do not account for the intangibilities of the human element. Audiometry, it must be remembered, is largely a subjective test unless one resorts to the "conditioned reflex" methods of the animal experimenter. As a matter of fact, in the following paper, Dr. Guilder states that she has successfully used that method in her work on preschool children. Far more applicable in crusade work against deafness are the so-called "group audiometers," which have been used for some years in the public schools of Massachusetts and other states. The group audiometer consists of a phonograph with an electric pick up to which as many as forty earphones can be connected. The disks

used in the phonograph are carefully made recordings of monosyllables or numbers, which the pupils must write down as they hear them. Any pupil whose record sheet shows more than the permissible number of mistakes is then given a note to the parents advising them of the fact that the child has a hearing defect, and that they should consult their family physician, who refers the patient to an otologist or an ear clinic, where more accurate tests can be made. Rough as the group audiometer test, also called "screen test," may be, it is surprising how frequently even very slight losses of hearing are being detected. It can safely be said that in the majority of such cases the hearing loss is entirely unsuspected by parents and teachers alike, to say nothing of the patient. It stands to reason that such a program of deafness detection is of the greatest service to the public, and it is to be hoped that ultimately all the states of the Union will avail themselves of the systematic use of the group audiometer in the public and other schools.

The electric audiometers just described are obviously not adapted for the purpose of the busy general practitioner, who must have more easily available means for testing a patient's hearing. Undoubtedly, the oldest and, for all practical purposes, the most valuable of these is the human voice. The voice test has of late (since the introduction of the electric audiometer) been much maligned as being "unscientific and inaccurate." It must not be forgotten, however, that the human voice is more important to the human ear than any other sound. In general practice, it is much more essential to determine quickly and roughly the hearing acuity for the voice than to measure it "accurately" in terms of cycles and decibels. Two types of voice are usually and properly employed: the whispered and the conversational.

Of the two, the whisper is the more reliable because, as a rule, it is easier to keep it on a fairly even intensity level. A few simple rules should be observed. A "stage whisper" is not permissible.

*Assistant Surgeon, Massachusetts Eye and Ear Infirmary; Assistant in Otolaryngology, Harvard Medical School.

of such a program. The Foundation is most grateful for the co-operation of all who have made this beginning possible: the clinic staff, the social-service staff, the three highly trained teachers who volunteered their services so that the technics of therapeutic teaching might be worked out, the several hearing aid firms who have met the special needs of the project so efficiently, and all who have referred these young people to the clinic.

On the basis of experience at the Winthrop Foundation, the following problems are briefly discussed: the gravity of the handicap as it appears in the cross-section of New England children studied; the hearing study and its adaptation to the different age levels; and the program for remedial guidance and its adaptation to meet the needs of the individual child.

Gravity of Handicap

A hearing defect of any degree, even the slighter deviations from normal, may be seriously handicapping in early childhood, because of the vital part that hearing plays in the child's speech-language development, in his early intellectual growth and, later, in his education.

His first efforts at speech are an imitation of what he hears. If the sound of voice fails to reach him, he will not develop speech until taught by visual and kinesthetic methods.* If speech is a blur of confused sounds to him, his first efforts at imitation will be delayed and quite imperfect, but will gradually improve as he learns to listen more carefully. His first words may consist largely of vowel sounds. If, as in children with some of the slighter high-tone deviations, he fails to hear only the soft, high-pitched consonant sounds, these sounds will be added slowly and imperfectly, and he may substitute one consonant for another. Frequently, the speech defect so predominates the picture that the underlying hearing impairment may go unrecognized for a number of years.

The young child with even a slight reduction in hearing ability increases his vocabulary more slowly than his normal playmates, and may seem in various ways retarded because of the restriction of his auditory field, even though he has a good intellectual endowment. The child whose hearing distance is only two or three feet misses all the innumerable opportunities of acquiring new words and new facts that make the young child's mental growth so incredibly rapid. If the hearing distance is increased, an intelligence quotient, based to any degree on an understanding of language, is often raised in a short time.

Too much can scarcely be said about the handicapping effect of a hearing disability of any degree

during school years. Such disabilities certainly rank high among the tragedies of school children at present. They are one of the principal causes for the repetition of grades. They are responsible for many of the behavior problems of childhood and adolescence. The child may have been taught to read the lips, but he still loses his place when the children behind him are reciting; he fails to understand the spelling words or the test questions, if the teacher happens to move to another side of the room.

It is therefore apparent that, from the age of twelve months and on through the preschool and school years, a hearing impairment of any degree is a serious disability, and even the slighter ones are far more handicapping than similar degrees of impairment occurring for the first time in adult years. The adult has years of experience in listening, and is often able to supply the word or sound that he does not quite hear, whereas the child is constantly being presented with unfamiliar words and strange new facts.

In addition to the effect of the handicap on early development and education, many pleasures are denied the child with a partial hearing disability—all the soft sounds indoors and outdoors, such as the singing of birds, the chatter of children, the rumble of the city traffic and the sound of a distant airplane. It is hard to forget the eagerness of a little boy who rushed to the door during his first hearing-aid demonstration and stood enthralled at the sound of the cars whizzing by—or of the five-year-old girl who was so surprised at the sound of the chatter of the other children when she first wore her hearing aid to kindergarten.

Hearing Study

To evaluate the child's hearing defect in terms of hearing ability and disability, which may serve as a basis for the clinic remedial program and for interpretation to the family and the teacher, the hearing test has been converted into a hearing study.

For the *child of school age*, one must know not only the character and degree of the hearing impairment in terms of a pure-tone audiometer test by air and bone conduction and of tuning-fork tests, as described by Dr. Mueller in the preceding paper, but also the amount that he is handicapped in hearing of monosyllables, sentences and new school material, such as he might have in school the next day. This estimate is made in two ways: by a phonographic attachment to the audiometer, the amplification necessary in each ear for the child to hear a list of fifty words correctly is determined; and by voice, his unaided binaural hearing for

*This group constitutes a very small proportion of the total number, and is provided for in schools for the deaf.

words, sentences and school material is studied and his hearing distance for different types of material, as well as for individual speech sounds, is established. In this way, one can determine how much difficulty the child has, when he is unable to read the lips of the teacher or of the child who is reciting behind him. All these procedures are necessary, because throughout the years of childhood, there is often not a perfect correlation between the pure-tone test and the interpretation of words heard, which is a function of the higher cortical centers. These various technics are adapted to the age level of the child. Speech defects are recorded as noted. The hearing study is an excellent opportunity for interpretation of the child's difficulty to him and later to his parents.

For the *preschool child*, the entire study is carried out in a nursery-school setting, with play material and with an observation and play-conditioning technic. The child's spontaneous responses to voice, music and a number of gross sounds of different pitches are first studied, and then his trained response, by conditioning him to "pump a ball" or "jump a horse" when he hears a bell or a drum tap. Later, the same procedure is used with the word "pump" or "jump," and in this manner his hearing distance for conversation and whispered voice can be determined, even though he has only a limited understanding of language or none at all. A word-picture game is used for the study of his interpretation of language, and speech is encouraged by play telephone conversations. The audiometer test is introduced as early in the program as possible. A word-picture method is often used up to the age of eight years for study of the child's ability to hear speech.

Remedial Guidance

No one group of the major handicaps calls for more highly individualized remedial programs, based on a detailed study of the child's ability and disability, than the hearing defects of childhood. Yet in no group has the remedial program been more generally routine. The day is past when the routine recommendation of lip reading to every child with a hearing handicap is sufficient. The clinic's duty is not completed at that point: these children deserve the best that medicine and science can give them, and their future happiness and efficiency depend on the proper remedial program at the proper time.

The initial rehabilitation should be considered a therapeutic procedure, growing out of the individual child's needs as evidenced by the cumulative study of his abilities and disabilities in hearing, speech and language during the period of clinic observation, study and therapeutic teaching. The

preschool child remains a rehabilitation problem until satisfactorily launched on his school career. The child of school age should remain a clinic rehabilitation problem until he and his parents understand the nature of his handicap and until he has gained self-confidence and become master of the situation by realizing that he is on the road to better hearing. In the clinic, the child is willing to discuss his difficulties, because he comes to tell his troubles, and it is one's responsibility to see that he is equipped to overcome them to the greatest possible degree. In school, he tends to make light of his handicap, and various behavior problems grow out of his effort to cover his real sense of inferiority.

The majority of these children can be given better hearing and, through better hearing, can acquire better speech, better language and an equal opportunity for school progress and for happiness in and out of school. How is one to accomplish this?

When hearing begins to fail, the eye naturally begins to help out the ear by interpreting some speech sounds through watching the movements of the lips. The soft consonant sounds, which are usually the most difficult to hear, are the easiest to interpret on the lips. Therefore, the eye should always be trained to help the ear whenever there is a permanent hearing defect sufficient to interfere with the hearing of speech. Lip reading is thus one of the first of the remedial measures advised, but it should always go hand in hand with the greatest possible use of hearing, so that a hearing aid, as well as lip reading, is advised when the unaided ear cannot easily hear the louder speech sounds. It has been proved conclusively that sight and hearing together give the highest percentage of speech intelligibility at every age level. In addition to these measures, children whose hearing handicap has been present during early childhood need help with speech and language.

For the *slighter hearing defects in children of school age*, lip reading should be recommended if the child's audiogram shows a persistent loss of between 20 and 30 decibels in the speech range, or if his hearing distance for monosyllables, sentences or new school material is less than 20 feet. This will usually be sufficient for the child whose loss occurs at the age of twelve years or over, and he can proceed with the study of lip reading at school, with instructions to return to the clinic for periodic hearing check-ups and further advice concerning remedial measures, if the hearing impairment proves to be progressive. As always, parent and child are made to realize that hearing, like vision, teeth and general health, should be

checked at intervals, that good hearing is one of the most precious endowments and to be carefully guarded, but that the deviations from normal hearing are no rarer than visual defects and that a hearing defect should never be a cause for hypersensitiveness. For children from six to twelve years old, listening exercises on a game basis should

weeks, he is ready to wear his hearing aid to school and to continue the study of lip reading at school. The class is therefore a revolving one, with a nucleus of old pupils and new ones entering whenever they come to the clinic.

Such a program has proved to be the only satisfactory way of meeting the psychologic and tech-

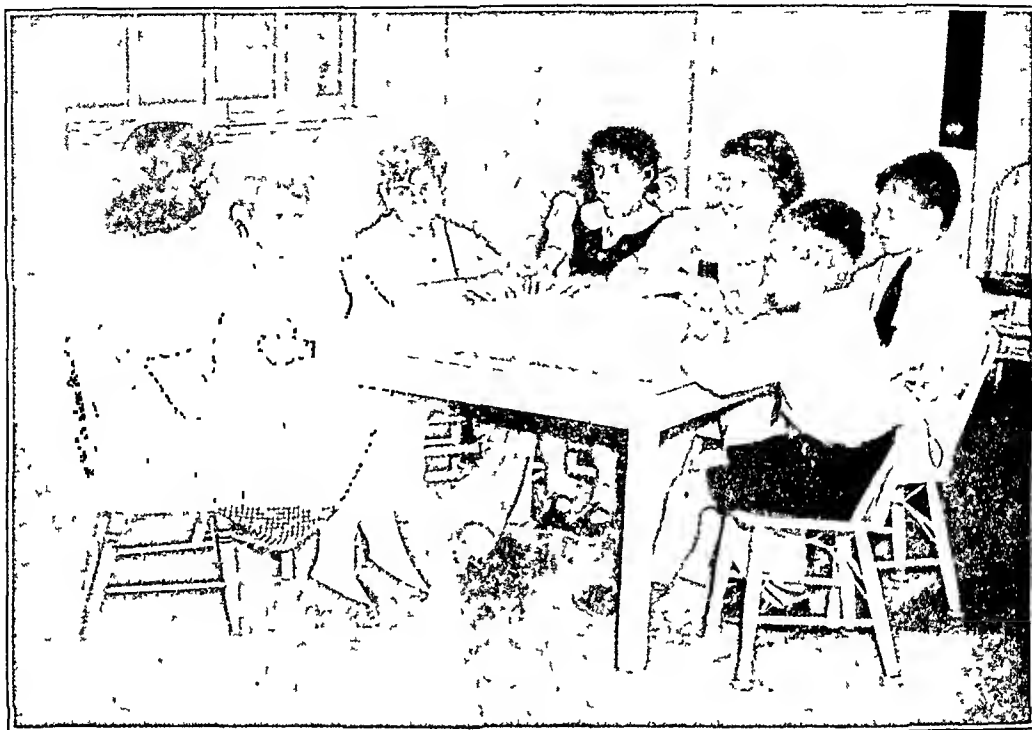


FIGURE 1.

This photograph shows a group of children having their first training in listening with hearing aids

be encouraged. Many of these children acquire auditory inattention, because conversation at a distance becomes blurred to them. Parents often describe them as "heedless." They should be advised to make listening fun for the child, and the child himself should be urged to listen carefully.

For the *hard of hearing and partially deaf group over twelve years of age*, whose audiograms show a persistent loss of more than 30 decibels in the speech range, and whose hearing distance for monosyllables, sentences and new school material is less than 15 feet, a vacuum-tube hearing aid, the study of lip reading and attendance in a clinic class are recommended. In the clinic class, which is taught by a lip-reading teacher, the child has an opportunity to see other children using aids; he gains practice in adjusting his aid and in combining sight and hearing satisfactorily through exercises, guessing games and pleasant conversation. Most important of all, he has a good time, gains self-confidence, and is better able to cope with his handicap. After attending the class for six to eight

nical problems of adjustment to the new vacuum-tube aids, and the plan is in accord with therapeutic training classes for other types of disabilities in children and young people. Many in the group from twelve to eighteen years are now wearing their hearing aids satisfactorily in school and for outside work and social activities. The majority acquired a hearing distance of at least 20 feet with their aids. In some cases, the remedial program has prevented impending school failure and has made it possible for a high-school boy or girl to go on with his or her chosen line of training. Every effort is made to help this group overcome their hypersensitiveness, and the things to be done to acquire better hearing are constantly stressed, rather than the seriousness of the handicap. As the program for better hearing has grown, parents, children and young people have helped spread this feeling of hopefulness to the newcomers. Despite the combined efforts of the clinic and social-service staffs, however, some parents and some children and young people refuse to accept the idea

of a hearing aid. For them, there are psychological obstacles that will be overcome only through the further education of the public to the fact that today a large majority of the children with hearing handicaps can be completely rehabilitated, and that a hearing aid is by no means a sign of lowered efficiency or ability.

The *hard of hearing and partially deaf group six to twelve years of age* present more complicated individual remedial problems. Many have developmental, high-tone defects with the characteristic speech defects and varying degrees of retardation in language development. Some have conduction losses going back to early childhood, with a large amount of rapid but imperfect speech. Many of these children were late talkers, and have continued to reproduce speech imperfectly as they have heard it. These children need the stimulus of clinic class work (Fig. 1), as described above, but they also need individual instruction in speech correction, lip reading and listening exercises by a specially trained teacher. After several months of weekly clinic training, both individual and group, these children are ready to wear their aids satisfactorily in school, and should be able to proceed in public school with the help of special lip-reading instruction, which many school systems provide. A number of these children, without the benefit of a hearing aid and the intensive remedial clinic program, would have been obliged to transfer to a special school for the deaf. It is hoped that a considerable group are being completely rehabilitated. This means that some children will be able to remain in their own homes and in regular classes who formerly were transferred to special boarding schools at considerable expense to the State. Such programs, therefore, organized on a larger scale, can be measured in terms of greater happiness to a group of children and parents, greater efficiency in the coming adult generation and an appreciable financial saving to the State.

The *preschool group* present very special remedial problems. The preschool child with only a slight hearing handicap may have very poor speech, and is usually a very poor listener. At certain times during the day, he may seem not to try to listen. Speech may be so blurred and confused to him that he does not make the effort to listen when he is tired. If his hearing distance for familiar words is 10 to 12 feet, he should be trained and encouraged to listen through games and exercises, which he will enjoy. His imperfect speech sounds should be corrected through hearing to as great an extent as possible, and he should have some training in lip reading, but with emphasis always on the combination of sight and hearing. His clinic program should consist of both group

and individual work, and the listening exercises and games should also be carried out at home.

For the partially deaf preschool child, who has developed a small amount of imperfect speech and who has a hearing distance of from 2 to 12 feet for familiar words, a hearing aid, in addition to in-



FIGURE 2.

This photograph shows how learning to listen and to lip-read are made fun for young children.

dividual training in listening, lip reading and speech correction through hearing, is recommended. Again, the stress is placed on a combination of sight and hearing. The entire program, from the hearing study throughout the training period, is carried out on a play-school basis. The group class often seems like a party to these younger children (Fig. 2). The hearing aid is first introduced as a play telephone, and a word-picture game is used for measuring its usefulness at various distances.

A five-year-old girl has been wearing an aid the entire day for six months. She has worn it in kindergarten as unconsciously as a child might wear a pair of glasses. Her hearing distance has been increased from 2 feet to 15 feet, and she has

lowered the pitch of her voice, corrected her own imperfect speech sounds, and increased her vocabulary from about thirty words to sufficient language to carry on a normal conversation for her age. She is now able to take part in games, whereas formerly she stood on the outside and watched. Being fitted to an aid at just this crucial moment, she should have a normal school career and a much happier, fuller childhood.

If the age of rehabilitation can be lowered to three years, still more of the critical years of early childhood may be retrieved, and speech and language may be acquired more completely in those years of greatest speech readiness. The detection, evaluation and correction of hearing disabilities during preschool years are a major aspect of the entire problem. A year of childhood lost can never be completely regained. The child is normally most ready to acquire speech and language during his second, third and fourth years, and should be ready at six years to grasp new material rapidly through his hearing. More stress should be placed on the hearing readiness of children before they enter school, and greater efforts made to cor-

rect, through proper remedial measures, defects that cannot be cured through therapy. As the mother of a five-year-old child said, "Next to complete restoration of hearing, H——'s complete adjustment to her hearing aid is the nicest thing that could have happened to us."

SUMMARY

With increasing emphasis on the early discovery of physical defects in children, a great need arising in the field of otology for the development of intensive clinic programs for the detailed study of the abilities and disabilities of children with hearing handicaps, adapted to the different age levels, and for the development of programs of therapeutic remedial guidance, based on such individual studies. The majority of children with hearing handicaps are potentially normal, if found early and adequately rehabilitated. Better hearing is now a possibility for most of these children, and, because of this, better speech, better language and an equal opportunity for progress in school and for happiness in and out of school.

243 Charles Street

THE WORK OF THE BOSTON GUILD FOR THE HARD OF HEARING

EUNICE ACHESON PUGH*

BOSTON

IMPAIRMENT of hearing is a serious physical defect as well as a social, economic and vocational handicap to a vast number of people. Surveys throughout this country indicate that there are approximately 15,000,000 persons at the present time with some hearing deficiency. This figure includes those with only a mild hearing deficiency and a large number of younger persons who readily respond to treatment. Nevertheless, it leaves several million with a permanent and serious hearing loss who cannot be helped medically and who are in real need of readjustment.

Many of these are hopeful cases, owing to the availability of agency services and a better understanding of hearing problems. It is therefore of real value for physicians to know about the local centers that serve deaf people and to become more familiar with the programs that enable the hard of hearing to remedy and surmount their difficulties.

The Boston Guild for the Hard of Hearing, located at 283 Commonwealth Avenue, is a social agency operated by and for the hard of hearing of

Metropolitan Boston. It offers its services not only to its members but also to the community by helping the person with a hearing loss to develop his remaining capacities and to make adjustment along a number of concrete lines.

One outstanding activity of the Guild is hearing-aid guidance service. The first step taken when a person comes for help is to study his particular case. To do this, several pertinent questions are always asked. Has he received adequate care from an otologist and has his hearing been given all the benefit of medical treatment? If not, medical advice is recommended either by an ear specialist of the patient's choice, by one of the Guild's consulting otologists or by the service of a dispenser, as the case indicates. Many persons are referred directly from physicians or hospitals, and in these cases a summary is frequently sent in advance. The second question asked is, What is the degree and character of the hearing loss? If this has not already been determined by an otologist, the Guild is prepared to make an audiogram, using a standard audiometer. If it is found that a person will be benefited by and is able to finance a hearing

*Executive secretary, Boston Guild for the Hard of Hearing.

ing aid, the next question is, Which of the several types and makes are most suitable? Laboratory evaluations of these instruments are not available to the average purchaser, but the only instruments in the Guild demonstration collection are those approved by the Council of Physical Therapy of the American Medical Association. It is believed that there is no best hearing aid for everyone, and an hour's comparison of the various instruments is an effective means of deciding which device assists the patient to make use of his impaired hearing to the fullest possible extent.

After one of several hearing aids is selected as giving the best results, the person is advised to consult the company where the instrument may be tried out and purchased. Every year, an increasing number of otologists and general practitioners refer patients to the Guild. This service aids the physician in overcoming the patient's habitual resistance to wearing a hearing aid and is a help to the person bewildered about which instrument to purchase among those so widely advertised.

In addition, the Guild has a few hearing aids that are available as loans to persons who are prevented by hearing difficulties from obtaining and maintaining employment and who have no means of financing an instrument.

Lip reading is another means of rehabilitating the deafened. Almost anyone whose vision enables him to see a speaker's lips at a distance of three or four feet can learn something about lip reading. The amount he learns depends on his attitude toward his handicap, his perseverance and his regular attendance at classes. The slightly hard of hearing can profit fully as much as the severely deafened and should be urged to take up the study of lip reading early, for this skill develops only gradually and with much practice. Hearing aid salesmen often say that the most successful users of instruments are those who have learned to concentrate their attention on the speaker's mouth as a result of lip reading lessons. It is therefore essential to stress the study of lip reading as well as the use of a hearing aid. The former also offers a solution to the person who cannot be helped medically and who is unable to hear with an audicle. Lip reading bridges the gap for the person whose loss is not severe enough to warrant the use of a hearing aid.

The Guild is not a school of lip reading, but gives classes in practice and drill, so that anyone who wishes to master the art is urged first to take private lessons from qualified teachers. It has free afternoon and evening classes, however, for those who cannot afford tuition elsewhere.

Another service is conducted for children with hearing difficulties by the giving of audiometer tests. Parents are also advised about adequate educational provisions for the child who is so handicapped. Always alert to outside contacts, the Guild interests school and health authorities in hearing tests for school children so that preventive and helpful measures may be taken in time. It owns a 4C audiometer, especially designed for the testing of school children in groups of as many as forty, which is available to any public or private school on the payment of a small upkeep charge. A trained audiometer technician on the Guild staff is also available to do this testing in the schools.

Massachusetts has its own department of vocational rehabilitation and a division for the hard of hearing under a trained social worker, who cooperates with the Guild in securing retraining and employment for many people.

The Boston Guild is also a service club offering a varied social and educational program to its members. This was founded on the premises that the isolation of the hard of hearing is largely responsible for traits often attributed to them—sensitiveness, suspicion, lack of courage and initiative—and that the cure lies in the removal of the cause. Entertainments, lectures, card parties, teas, out-of-door trips and gatherings for various other purposes provide incentive for people who are hard of hearing to get together and make new friendships. Special facilities, including a group hearing aid in the auditorium at the Guild House, make the programs easily available for the members. Men are encouraged to join a very active men's club, and young persons find worth while outlets in the young people's group.

The Guild also offers opportunity for growth in personality and creates normal outlooks with the right perspectives on unpaired hearing. Otologists with patients who are isolating themselves and who need a better attitude toward their handicap would do well to recommend membership in the Guild. Those who wish this privilege, however, should not belong to the deaf group, since facilities for them are provided elsewhere. Nevertheless, any deafened person may make formal application for membership at the Guild if he furnishes the necessary references.

Many people with normal hearing, among them physicians, not only support the Guild's work but become members. In no other way can they understand the urgent problems of hearing that are rapidly becoming more crucial in modern society.

The Boston Guild for the Hard of Hearing is supported by membership dues, by rent from rooms

in its house, by voluntary contributions from members and friends, by interest from endowments and by participation in the Greater Boston Community Fund campaign.

During National Hearing Week, the last full week in October, the local chapters bring their work and that of the American Society for the Hard of Hearing to the attention of the general public by radio talks, lectures, pamphlet material, posters, demonstrations of lip reading and publicity

of various kinds. Otologists and physicians are welcome to any of these activities.

There are eleven leagues for the hard of hearing in Massachusetts and thirteen in four other New England states, all of which are constituent chapters of the American Society for the Hard of Hearing and work actively in the interests of persons so afflicted.

283 Commonwealth Avenue

CASTRATION FOR CARCINOMA OF THE PROSTATE*

Report of Forty-One Cases

C. H. NEUSWANGER, M.D.,† AND VINCENT VERMOOTEN, M.D.‡

NEW HAVEN, CONNECTICUT

THE report of the effect of castration on carcinoma of the prostate by Huggins et al.§ before the meeting of the American Urological Association in June, 1941, at Colorado Springs so impressed us that we have urged all our patients with carcinoma of the prostate to permit a bilateral orchidectomy. To date, we have operated on 41 of these patients, none of whom, up to the present, have regretted having the operation done. One patient died of pneumonia five months after operation. In the remaining cases, there are no complaints. On the average, the patients gained a minimum of 5 pounds in weight, and many as much as 20 or 30 pounds. The most striking changes observed were a marked increase in appetite, complete relief of pain, improvement in bowel habits and a feeling of well-being. There was also complete relief of urinary symptoms, but all patients except 1 had also had a transurethral resection of the prostatic carcinoma, which, no doubt, contributed considerably to this improvement as well as affording an opportunity to confirm the clinical diagnosis.

Our observations substantially confirm those reported by Huggins and his co-workers, even to the almost miraculous response of one patient who had a paraplegia resulting from a metastatic lesion in the spine.

In the following cases, the results were striking.

CASE REPORTS

CASE 1. G. A. P., when first seen in March, 1940, was found, on rectal examination, to have a carcinoma of the prostate. Except for nocturia once and some slight day frequency, he had no symptoms of note. In May, 1941, the nocturia had increased to three or four times, and the fre-

*Presented at a meeting of the New England Section of the American Urological Association, Boston, February 12, 1942.

†Assistant clinical professor of surgery, Yale University School of Medicine.

‡Assistant clinical professor of urology, Yale University School of Medicine.

§Huggins, C., Stevens, R. E., Jr., and Hodges, C. V. Studies on prostatic cancer. II. The effects of castration on advanced carcinoma of the prostate gland. *Arch. Surg.* 43:209-223, 1941.

quency during the day to once every hour or so. The patient was not seen again until the end of September, 1941, when he had developed complete retention of urine, with overflow incontinence. He was immediately admitted to the hospital.

Rectal examination showed a huge prostatic carcinoma, which had occluded the urethral lumen to such an extent that it was not possible to pass even a filiform guide through it. Bilateral orchidectomy was done the next morning, no attempt being made to relieve the urinary retention.

Within 48 hours, the patient was voiding small quantities spontaneously, and by the end of a week, the bladder, which had previously been distended to the umbilicus, could not be felt or percussed above the symphysis. At present, the prostate is greatly reduced in size, although not yet within normal limits. The patient is able to empty his bladder completely and voids only twice at night. He has gained 22 pounds in weight and is symptom free.

CASE 2. L. J., a 77-year-old man, was seen during the latter part of November, 1941, complaining of priapism, which had begun about 3 months previously and was continuing for longer and longer periods without relief. He had no other symptoms or discomforts except that he claimed that intercourse made the priapism worse and more painful.

Rectal examination revealed a large, hard, nodular, carcinomatous prostate.

Following a transurethral resection (to obtain tissue for microscopic examination) and a bilateral orchidectomy, the priapism gradually subsided until the 4th postoperative day, when the penis was completely flaccid, in which condition it has remained ever since.

CASE 3. D. M. D., a 76-year-old man, was admitted to the hospital for relief of respiratory distress in September, 1941. In March, 1936, one of us (C. H. N.) had operated on him, doing a radical prostatectomy and seminal vesiculectomy for carcinoma. Since that time, he had been considered cured. It was learned, however, that owing to marked respiratory distress he had been bedridden for 3 months.

On admission to the hospital, the patient was practically moribund. X-ray examination revealed that the lung fields were riddled with metastatic carcinoma, as were the bones of the pelvis, the lumbar and dorsal portions of the spine and the ribs. The patient had no urinary symptoms, and there was no local recurrence of the carcinoma.

Since it was assumed that the metastatic growths were from the old prostatic carcinoma, a bilateral orchidectomy was performed under local anesthesia. The general condition rapidly improved, so that the patient was able to go home at the end of 2 weeks. Five months later (peritonitis), he was up and about most of the day doing odd jobs about the farm. His general health was greatly improved, and the respiratory distress almost gone.

CASE 4 W W, a 55-year-old man, was first seen on December 1, 1941, complaining of girdle pains which radiated from the back around and forward to the umbilicus, of 9 months' duration. These pains were noticed whenever he bent forward or stooped to lift anything. Soon, he noticed that the pain was more marked along the lower costal margin and he began to have aches and pains in the arms and shoulders as well. He thought this was due to nervousness and worry as the result of the death of his son. On the advice of a friend he consulted a chiropractor, who manipulated him for one course of thirty-five treatments and a second course of twelve during June, July and August. Since he did not get a great deal of relief, he was advised to have his teeth extracted. In September, he was sure it was all nerves and therefore consulted a neurologist, who had him admitted to the hospital for examination. Neurologic examination was essentially negative, but x-ray films revealed several dental root abscesses and widespread osteoplastic changes throughout the spine, pelvis and bony thorax probably metastatic from a carcinoma of the prostate. After having all his teeth extracted, the patient was sent home with the advice to his physician to give him what sedatives he might need.

Early in October, he began to notice frequency of urination and a month later found that he was not able to use his legs very well. He staggered when walking, and his legs felt weak. This condition gradually got worse until November 15, when, on returning home, he found that he was unable to climb up stairs. He was put to bed and soon discovered that, although he had a great deal of pain and tenderness along the lower rib margin, he had no feeling whatsoever from the waist down. He was unable to move his legs, which felt dead, and when he attempted to move them his wife noticed that they were quite stiff. The next day, he was unable to urinate and therefore called his physician, who catheterized him. This was done twice a day until admission to the hospital on December 2.

On entry, the patient had a spastic paraplegia, with complete loss of sensation to pinpricks from the waist down. There was a band of hyperesthesia just below the costal margin, and he was unable to distinguish between heat and cold on the left side.

On December 3, a transurethral resection of the prostate and a bilateral orchidectomy were done. The catheter was removed on the 4th day after the resection and the patient was subsequently able to void spontaneously. The bowels moved voluntarily, whereas before operation they moved only with an enema.

Two days after orchidectomy, the patient noticed involuntary twitching of his legs, with occasional jerking movements. A week after operation, there was a beginning return of sensation and some slight voluntary movement of the legs. Two weeks after operation, he had almost complete return of sensation from the waist down, and the area of hyperesthesia had practically disappeared. He was also able to move his legs freely in bed. A week later, he was up and walking about with crutches and had complete urinary and bowel control.

When seen on February 10, 1942, the patient had gained 25 pounds in weight. He was able to walk about wherever he pleased with the help of a single cane, which he considered unnecessary. He had no pain or discomfort anywhere, even on bending. He emptied his bladder completely, voided once during the night and once every 3 or 4 hours during the day. Neurologically, we could determine no sensory changes in the lower extremities. The muscle tone was good, and his knee jerks were equal and active. A mass of supraclavicular lymph nodes on the left, which were large, hard and readily palpable when first seen in December, are now definitely much smaller, and the prostate is considerably reduced in size. Microscopically, the tissue resected was reported to be adenocarcinoma of the prostate, Grade II.

Comparing the x-ray films taken 2½ months before orchidectomy with those taken 2 months after operation, one sees that all the lesions became much denser, giving the impression that the disease had become more widespread despite the very marked clinical improvement.

SUMMARY

A report is given on the early postoperative effects of bilateral orchidectomy and transurethral resection on 41 patients with carcinoma of the prostate. Four very striking cases are reported in detail.

PREMONITORY SYMPTOMS OF MYOCARDIAL INFARCTION*

NORMAN H. BOYER, M.D.†

BOSTON

SINCE 1912, when Herrick¹ first described the characteristic signs and symptoms associated with infarction of the myocardium, atypical cases have been recognized with gratifying frequency. Knowledge of the pathology, physiology and pathologic physiology of the coronary circulation continues steadily to advance. The treatment of myocardial infarction, once it has developed, is better understood and more generally applied. Knowledge has apparently progressed to the point where it may now be profitable to turn attention toward recognition of the premonitory symptoms of myocardial infarction in the hope that the institution of therapeutic measures may diminish the severity of the illness or even, in some cases, prevent clinically recognizable infarction entirely.

In a certain proportion of cases, probably a larger number than has been suspected, the onset of myocardial infarction is not sudden and unpredictable but is preceded, for a variable time, by premonitory symptoms, which should receive more serious and general attention. The following cases will serve to indicate some of the danger signals of impending myocardial infarction. Some of the cases furnished a hopeful hint that favorable effects may be expected by prompt recognition and institution of measures designed to increase the absolute or relative coronary blood flow.

CASE 1. A 58-year-old man had noted slight exertional dyspnea for about a year. For 3 months, he had had mild substernal pain, usually after meals. He then began to have attacks of severe, crushing substernal pain, not related to effort and lasting 2 or 3 hours. He had four such attacks in the course of a week. He was seen by his physician several times during that week, and each time the electrocardiogram, white-cell count and erythrocyte sedimentation rate were within normal ranges. Other studies revealed no extracardiac cause for the pain. The patient was advised to go to Florida for a vacation, but 2 days later, he developed a severe attack of pain lasting 8 hours. With this attack, he went into collapse and remained in "shock" for 3 days, with oliguria and rising blood nonprotein nitrogen. The development of fever, leukocytosis (a white-cell count of 18,000) and characteristic changes in the electrocardiogram confirmed the diagnosis of acute myocardial infarction. The course was somewhat stormy, with paroxysmal auricular fibrillation and at least one splenic infarct. However, after 8 weeks in bed and 2 months more of easy convalescence, the patient made a good recovery and has been well and active for the past 2 years.

In this case, the significance of the repeated prolonged attacks of chest pain during the week preceding acute infarction was not at the time fully appreciated. The duration of the pain seemed to the physician in charge to be too long for angina pectoris, and the absence of fever, leukocytosis and electrocardiographic changes apparently eliminated infarction. It was concluded, therefore, that the heart was not the seat of the pain. Had more attention been paid to the preceding story of substernal pain after meals, it is likely that the prolonged attacks would have taken on new significance. Prolonged substernal pain, with or without characteristic radiation and with or without antecedent angina pectoris, should, in the absence of other obvious causes, be regarded as due to sudden narrowing or closure of a coronary artery. Care must be taken, of course, to avoid confusion with acute coronary insufficiency induced by tachycardia or some other cause.

It is still not widely enough appreciated that the clinical evidence on which proof of the diagnosis of acute coronary occlusion depends consists in manifestations of actual infarction of the muscle. Coronary occlusion and myocardial infarction are not synonymous terms; either may occur without the other, but it is only infarction that produces fever, leukocytosis, changes in the electrocardiogram, friction rub and so forth.

CASE 2. A 58-year-old man, whose family history was unfavorable inasmuch as his mother had died of angina pectoris at 53 and his father of coronary occlusion at 55 years of age, suddenly developed, on March 4, 1941, discomfort over the precordium, with radiation to the back and to the neck. On one or two previous occasions, a similar but less severe and less prolonged pain had occurred. The patient was admitted to the hospital within an hour of the onset, but the pain persisted for several hours despite bed rest and morphine. Physical examination was negative except for occasional premature beats. During the first day in the hospital, two intramuscular injections of papaverine hydrochloride, ½ gr., and atropine sulfate, 1/100 gr., were given at four-hour intervals. Two days later, the pain returned for a few moments following a bowel movement. The patient was kept at rest in the hospital for 2 weeks, during which there was no fever, leukocytosis or increase in sedimentation rate, and no abnormalities or serial changes in the electrocardiogram. He continued to rest at home for another 3 or 4 weeks and has been well and active for the past year.

This appears to be a case of sudden coronary narrowing or occlusion without definite clinical evidence of infarction. Such cases are being recog-

*From the Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

†Instructor in medicine, Boston University School of Medicine; assistant physician, Evans Memorial, Massachusetts Memorial Hospitals.

nized with increasing frequency. It seems wise under such circumstances to put the patient at rest, to keep the needs of the heart muscle at an absolute minimum. The use of papaverine is based on its apparent good effects when there is sudden closure of a peripheral artery or embolism to a

Not only must one be alert to the possibility of occlusion or narrowing of a coronary artery, without clinically demonstrable infarction on the corresponding myocardium, but also one must guard against haste and impatience in the management of such patients. Failure to provide an

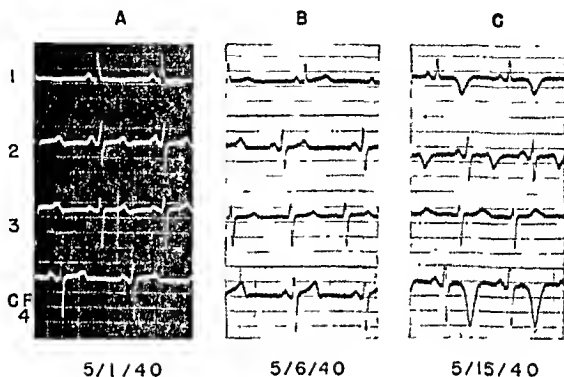


FIGURE 1. Case 3.

Record A was taken twelve hours after a severe attack of substernal pain lasting several hours, there is a considerable degree of left-axis deviation, slight inversion of T_1 and an upright T_3 , with a slightly high origin of ST_3 ; the record was interpreted as indicating left ventricular strain. Record B, taken five days later, shows slight changes in the T waves and ST segments; the record is not definitely abnormal. Record C was taken fourteen days after admission and the day following a trip to the X-ray Department for a gastrointestinal series; the tracing shows marked inversion of the T waves in Leads 1, 2 and 4.

pulmonary artery. There is evidence that sudden closure of an artery to any part is often accompanied by reflex vasoconstriction of other vessels to that part. Such reflex vasoconstriction in the heart might well interfere with the establishment of collateral circulation, most if not all of which comes from the unoccluded coronary vessels.^{2,3}

The presence of reflex constriction of the coronary bed following ligation of one of the coronary arteries has been indicated by the experimental studies of Manning, McEachern and Hall⁴ and LeRoy and Snider.⁵ The latter authors were able to reduce the mortality of coronary-artery ligation in dogs by the use of atropine, which they believe interrupted the efferent pathway of the reflex arc. McEachern, Smith, and Manning⁶ were able to show a moderate reduction (from 75 to 50 per cent) in the immediate mortality of coronary-artery ligation following the administration of papaverine in doses rather larger than are ordinarily employed clinically.

adequate period of rest may result in delayed infarction, such as presumably occurred in the following case. It hardly needs to be emphasized that the error of ascribing to the heart pain that belongs in the domain of surgery should be scrupulously avoided. A careful history and good judgment go far toward preventing such an error.

CASE 3. A 61-year-old woman with known hypertension for 12 years had been well except for slight exertional dyspnea until 2 weeks before admission to the hospital, when she developed burning substernal pain on effort and after meals. A week before admission, the pain increased in frequency and severity and even came on at rest on one occasion. The day before admission, the patient walked a mile to her doctor's office and on the way home developed a severe substernal pain, which gradually increased in severity and radiated to the arms. The pain lasted several hours, was only partially relieved by nitroglycerin, and was accompanied by weakness and sweating. On admission, the patient had no pain or other complaints. The blood pressure was 194/90. The heart was regular, the sounds were of fair quality, and there were no murmurs or gallop. The lungs were clear, and the abdomen

and the extremities normal. The temperature was normal, and the white-cell count was 10,000. The sedimentation rate, however, was elevated to 1.1 mm. per minute. The patient remained free of symptoms, fever and leukocytosis for 2 weeks. The electrocardiogram on admission showed slight inversion of T_1 and upright T_3 (Fig. 1). The pattern was thought to indicate "left ventricular strain." Five days later, T_1 had become upright. At the end of 2 weeks, the patient was sent to the X-ray Department for a gastrointestinal series because of the absence of any clear indication of myocardial infarction and because of the previously mentioned relation of the pain to meals. Following her return from x-ray study, she developed more pain, the white-cell count subsequently rose to 13,600, and the electrocardiogram showed deep inversion of T_1 , T_2 and T_4 . There was gradual evolution of the electrocardiogram toward normal in the course of several weeks.

The patient made a good recovery but succumbed to another myocardial infarction 1½ years later.

It seems fairly clear that this patient had coronary occlusion, following a short period of angina pectoris, but without definite evidence of infarction of the heart at the time of admission to the hospital. The untimely trip to the X-ray Department may have precipitated actual infarction of the heart by increasing metabolic demands at a time when the coronary blood flow could support resting needs only. The possibility of a sudden, unrelated occlusion cannot, of course, be summarily dismissed.

CASE 4. A 51-year-old man had always been well and very active. In December, 1941, he developed a mild sense of constriction beneath the sternum while riding horseback. The discomfort lasted a few moments. On two or three subsequent occasions, mild substernal discomfort recurred. On February 16, 1942, he developed a severe attack of chest pain lasting several hours. Fever, leukocytosis, and characteristic electrocardiographic changes established the diagnosis of acute infarction.

This case illustrates the fact, now fairly widely known, that myocardial infarction may appear soon after the onset of angina pectoris.

It seems reasonable to suppose that decreasing the demands on the heart, by bed rest during the critical period when collateral circulation is presumably being established, may have a salubrious effect. The possibility that this may occur is indicated by the following case.

CASE 5. A 69-year-old man had always been well and active until 10 or 12 days before being seen, when he began to have attacks of substernal pain that were brought on by walking and relieved by rest. Later, the pain was induced by eating. On the day of the examination, the pain appeared following lunch and was partly relieved by nitroglycerin, but the patient still had some pain when seen 2 hours later. Physical examination and fluoroscopy of the heart showed no abnormalities. The temperature was 99°F., and the white-cell count 10,000. The electrocardiogram showed depression of the ST segments in all leads (Fig. 2), a common pattern during spontaneous or induced attacks of angina pectoris.

The patient was hospitalized and kept at bed rest for 3 weeks, during which there was no fever, leukocytosis or increase in the erythrocyte sedimentation rate. The electrocardiogram taken 3 days after the first record showed no ST displacement. Another record a week later did, however, show changes in T_1 and T_3 , suggesting that the heart had not entirely escaped damage.

There is, of course, no proof that this patient would not have done equally well if allowed to continue with his usual mode of life, but this seems an entirely unreasonable assumption. Ex-

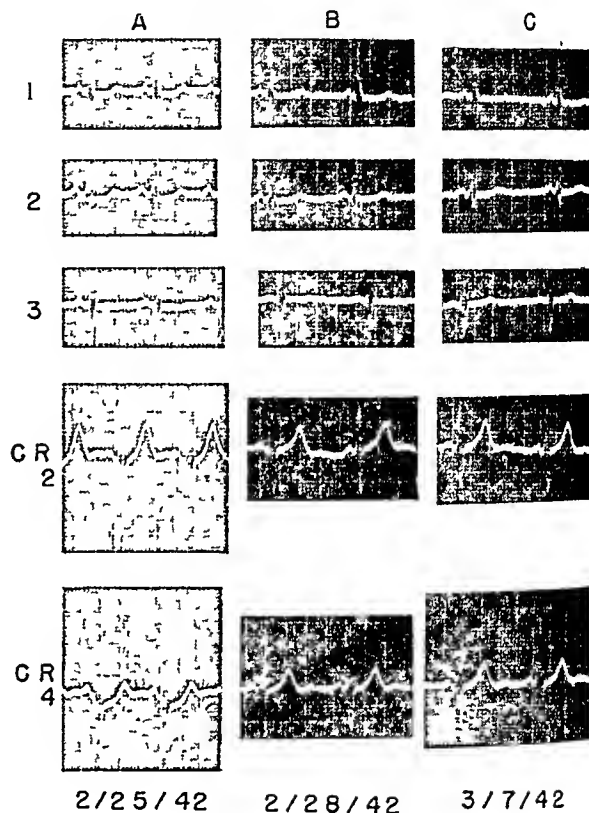


FIGURE 2. Case 5.

Record A was taken during an attack of pain lasting two or three hours; there had been sudden onset of angina pectoris ten to twelve days previously; the record shows depression of the ST segment in all leads. Record B, taken three days later, shows no definite abnormalities. Record C, taken seven days later, shows flattening of T_1 and an increase in the height of T_3 , suggesting that there had been some change in the heart muscle.

perience with other patients who have suffered extensive infarction of the heart soon after the sudden onset of angina pectoris or following prolonged pain (for example, Cases 1 and 4) leads one to expect a similar course in this patient. That such an infarction did not develop can be fairly attributed to lessening the demands on the heart by means of bed rest.

CASE 6. A 60-year-old man, who had had angina pectoris for 5 years, had a sudden increase in frequency and

severity of attacks for 2 or 3 weeks. During this time, the attacks occasionally came on at rest. There was no dyspnea or other cardiovascular symptoms. Physical examination and fluoroscopy of the heart showed no abnormalities. The electrocardiogram showed prolonged auriculoventricular conduction (a PR interval of 0.22 second) and right bundle-branch block. Because of the recent onset

pectoris, and at that time the electrocardiogram was normal. In January, 1941, he again complained of chest pain not characteristic of angina pectoris. The electrocardiogram had changed, however, T₁ being inverted (Fig. 3). The patient was advised to curtail his activities, and after a few weeks the pain disappeared. In December, he was seen again because for the previous week he had had dull

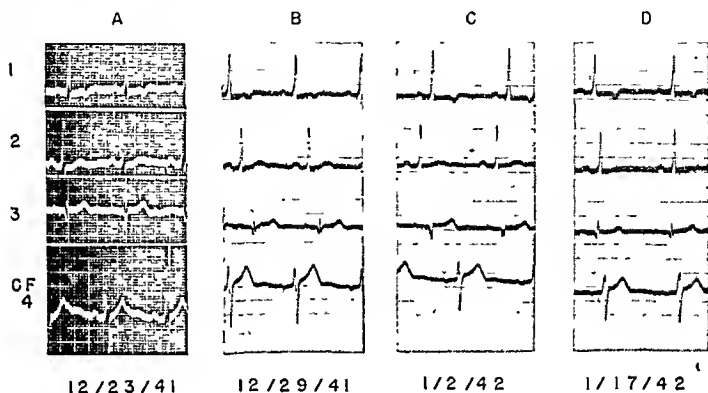


FIGURE 3. Case 7.

Record A, taken one week after the sudden onset of angina pectoris, is identical with one taken eleven months previously; the patient was admitted to the hospital at once because of the symptoms of coronary insufficiency; the record indicates left ventricular strain but not acute infarction. Record B, taken six days later, shows no essential change in the T waves or ST segments, the PR interval, however, has lengthened from 0.18 to 0.22 second. Record C, taken four days later, shows no change. Record D shows slight flattening of the T waves in Leads 2 and 3; the slight T-wave changes and prolonged auriculoventricular conduction suggested that active changes had taken place in the heart.

of increased coronary insufficiency, the patient was advised to go to bed. This he declined to do. Ten days later, he was seized with a severe attack of chest pain lasting 6 or more hours. Serial changes in the electrocardiogram, a temperature of 101°F. and a white-cell count of 18,000 established the diagnosis of infarction. There was marked gallop rhythm, accentuation of the pulmonic second sound, Cheyne-Stokes respiration and persistence of a shocklike state for 2 days. There was an attack of tachycardia, probably of ventricular origin, although there was no graphic proof. After 3 months, the patient was able to undertake moderate activity without symptoms.

Not only the sudden onset of angina pectoris in a patient previously well but also the sudden increase in frequency and severity of pre-existing angina may presage the onset of myocardial infarction. It is reasonable to suppose that reducing the metabolic needs of the heart during this period may avoid such a critical illness as this patient went through, either by preventing infarction or by materially reducing its size.

CASE 7. A 60-year-old man had complained of vague chest pain in 1937. This was thought not to be angina

pain beginning at the back of the shoulders and radiating beneath the sternum. This time, the pain was definitely brought on by exertion and relieved by rest. The electrocardiogram was unchanged from that taken 11 months previously. Physical examination was negative. The patient was put to bed for 2 weeks, and on being allowed up, he developed a moderately severe attack of dull substernal pain lasting 10 to 15 minutes. He was put back at bed rest for another week and then gradually allowed up, without any recurrence of pain. At no time during his hospital stay did fever, leukocytosis or increased sedimentation rate develop. The electrocardiogram, however, showed prolongation of auriculoventricular conduction and slight changes in the T waves, suggesting, as in Case 5, that the heart had not entirely escaped damage.

This is another case in which it is difficult to prove that anything was accomplished by enforced bed rest. The changes in the electrocardiogram indicate, however, that changes were going on in the heart, and it is certainly not unreasonable to believe that such changes were less extensive than they would have been were the patient actively engaged in his usual occupation during this period.

DISCUSSION

The presence of prodromal symptoms probably depends on the rate at which the occlusive process in the coronary vessels develops. Sudden complete closure of a large or moderate-sized vessel will undoubtedly result in immediate infarction of the corresponding myocardium. Atherosclerosis of the coronary arteries is a progressive disease, which is fortunately accompanied by the production of collateral circulation when the need arises. At times, the growth of collateral circulation is unable to keep pace with the progress of the disease, and when the disease is in the ascendancy, symptoms appear or increase. When symptoms are present, indicating that the disease is progressing rapidly, such as the sudden increase of angina pectoris and the onset of prolonged pain, it seems only reasonable to keep the metabolic demands of the heart at a minimum by strict bed rest. In all ischemic tissue, there must be a peripheral zone in which the balance of supply and demand of blood is at a critical point. A little more or less blood or a little more or less demand may mean the difference between viability and death of the tissue. Thus, one might at least expect that, even if infarction occurs, its size may, in some cases, be reduced by virtue of reduction in the demands of the peripheral zone under conditions of absolute rest. If the occlusive process develops slowly enough or if the area affected is small, necrosis of the muscle may not occur. ⁸ There would seem, therefore, to be little room for doubting the advisability, on theoretical grounds, of minimizing the demands on the heart at a time when symptoms suggest that its blood supply is inadequate, but whether or not any tangible benefit accrues is difficult to evaluate.

Sampson and Eliaser⁷ have recorded their experience with the frequency of prolonged attacks of pain, preceding by an interval of days or weeks the onset of infarction. They observed premonitory attacks in 29 patients. Seven patients who were put at bed rest developed infarction despite this precaution, and the mortality rate was not significantly different from that in the remaining patients, who were allowed up and about during the interval between the onset of the premonitory pain and the onset of the infarction. However, they emphasized that the series is too small to allow any conclusions on this point. They had observed 6 other patients, with a single prolonged attack of pain, who were put at bed rest and subsequently did not develop myocardial infarction. They were unwilling to believe, without further proof, that infarction had actually been forestalled. It is true that convincing proof is difficult to obtain, but cases such as Cases 5 and 7, in which slight

changes occurred in the electrocardiogram, indicate that changes were occurring in the heart muscle, and it is not unreasonable to assume that such changes might have been more extensive had the demands on the myocardium been greater during this critical period.

Feil⁸ also calls attention to the frequency of preliminary pain in myocardial infarction. He states that the pain recurred for an interval of from twelve hours to four weeks preceding infarction, and that he encountered it in 50 per cent of patients with myocardial infarction. He further suggests the point, which needs strong emphasis, that *a normal electrocardiogram does not rule out a developing infarction*. He recommends moderate restriction of the activities of patients during the stage of preliminary pain, but, in view of the gravity of the situation, this seems an inadequate compromise. Complete bed rest under these circumstances has also been urged by Blumgart, Schlesinger and Zoll.⁹

The enforcement of two to four weeks in bed for the patient in whom there is no proof of impending infarction, or proof that the patient will benefit in any way from a period of enforced rest may seem to be radical treatment. Balanced against the possible death of the patient from acute infarction, a prolonged illness extending from three months to a year or more, chronic invalidism, or, at best, a heart with a large myocardial scar, two or three weeks in bed, *if there is the least hope of preventing these sequelae*, seems conservative treatment.

The length of time required in bed varies from case to case. There is experimental evidence that effective collateral circulation requires from one to three weeks for its development.^{10, 11} Thus, as a starting point, two weeks should be considered the minimum length of time. It can then be lengthened, if necessary, depending on the patient's response to gradually increasing activity.

It is not suggested that all patients with angina pectoris need be put at bed rest, although even here there is evidence that a period of bed rest at the start of treatment of all patients with angina pectoris may do great good.¹² It is when symptoms of a sudden increase in coronary insufficiency develop that enforced bed rest is urged.

Emphasis has been placed on bed rest, but it is clear from the report of Sampson and Eliaser that rest alone does not prevent infarction in all cases. Other general measures should not be neglected. Primary among these are sedation and avoidance of tobacco. Cognizance should be taken of the increase in cardiac work incident to large heavy meals, and the dietary should be arranged around light foods in small amounts. Drugs al-

leged to dilate the coronary arteries occupy a position of secondary importance. There are reasons for believing that the stimulating effect of the xanthines may be undesirable.¹¹ Papaverine may be used for its possible effect on overcoming spasm in unaffected vessels that serve as the source of supply for the collateral circulation. Although it has been shown that the maximum collateral flow occurs only after several days or weeks, an immediate increase,¹⁰ although slight, may conceivably keep all or part of the ischemic myocardium viable if such collateral flow is not hampered by reflex constriction of the vessels that provide the source for collateral circulation and if, at the same time, the metabolic needs of the heart are minimized. Atropine may also be used on the basis of previously cited experimental work, although the tachycardia incident to its use may not be altogether desirable. So far as is known, papaverine has no undesirable effects on the heart.

SUMMARY AND CONCLUSIONS

Sudden onset of angina pectoris, sudden increase in the severity and frequency of pre existing angina pectoris, and prolonged chest pain without signs of cardiac infarction have been found to precede the onset of infarction in some patients.

Recognition of these warning symptoms and proper treatment by rest, sedation, avoidance of

tobacco and the use of papaverine may, in some cases, reduce the size of the eventual infarction or possibly forestall it entirely.

29 Bay State Road

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PROTEINURIA AND THE ASSOCIATED RENAL CHANGES*

WILLIAM DOCK, MD†

NEW YORK CITY

THE first observers of proteinuria, Dekkers (1694) and Cotugno (1765), theorized that it should occur in certain conditions, made a single observation that happened to verify their erroneous theories and thus missed the true significance of the phenomenon.¹ Cruikshank, Wells and Blackall² first made systematic studies, and by 1827, John Bostock,³ studying his own cases and those of Bright, had arrived at the main truths known today: albuminuria occurs in many circumstances, often "of a trifling nature"; the protein in the urine "possesses every property of that in the blood"; the specific gravity of urine from cases of chronic proteinuria is "less than that of the urine in the healthy condition of the system"; "the serum generally in these cases contains less albumin than in health", and "the blood exhibits a very great deficiency of albumin at the same time that we observe the mode by which it passes off from the system by means of the kidney."

The large, greasy yellow kidney found in many cases of Bright's disease, with edema had tubular changes characterized by desquamation, regeneration with mitosis and large amounts of lipid in the cells of the tubules. The changes seem not unlike those in the heart and brain injured by anemia, or in the liver injured by toxins or anoxia. Pathologists were impressed by the severity and constancy of the tubular changes, which they regarded as probably toxic in origin. They even suggested that proteinuria might be due to tubular injury or be produced by tubule cells, as mucus is thrown off by injured cells in the nasopharynx, bronchus or colon. Modern methods such as ultracentrifugation and electrophoresis,^{4, 5} and also specific biologic tests show that the albumin and globulin, which are always found together in proteinuria, are identical in their properties with molecules of protein in the plasma and are not to any appreciable degree derived from the tissues. Studies of fishes with aglomerular kidneys and of others with glomeruli have shown that without glomeruli

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†Professor of pathology, Cornell University Medical College

there can be no proteinuria,⁶ and protein can easily be demonstrated in the fluid about glomeruli in cases of proteinuria.⁷ Finally, staining methods developed at the Mallory Institute of Pathology, of the Boston City Hospital, have made it possible to show that demonstrable glomerular lesions occur in almost all cases of chronic albuminuria.^{8, 9} The problem of proteinuria therefore concerns, primarily, altered permeability in the glomerulus and, secondarily, the effects of this leakage.

Since much information is at hand on the functions of the kidney and on glycosuria and hemoglobinuria, a review of these facts may be useful. By measurement of the ratio of the amount of substance eliminated in one hour's urine to the amount of 1 cc. of plasma (Addis ratio, renal clearance), much has been learned about human renal function. Diodrast clearances are very high, for the tubules and glomeruli eliminate over 90 per cent of the substance as it passes from renal artery to renal vein; this gives a measure of renal blood flow—about 1500 liters a day for a man of normal size. Inulin and sucrose seem only to escape in the glomerular filtrate and to be but little reabsorbed by the tubules; clearance of inulin gives a measure of glomerular filtrate—about 180 liters a day for a man.¹⁰ Richards¹¹ and his co-workers have analyzed glomerular filtrates from mammals and amphibia, finding the glucose, as well as the chloride and urea, similar to that in the blood, whereas protein, if present at all, is only in minute traces, less than 30 mg. per 100 cc. All the glucose is reabsorbed so long as the plasma level is below 180 mg. per 100 cc., and the reabsorption occurs in the proximal convoluted tubules.¹² Above that threshold, glucose appears in the urine, and above 250 mg. per 100 cc., practically the entire excess escapes in the urine, whereas glycogen appears in the tubule cells in demonstrable masses.

Since hemoglobin has 97 per cent the molecular weight of serum albumin and is tagged with a prosthetic group that makes it easy to study, the investigator of albuminuria is naturally interested in the precise studies of Whipple and his co-workers.¹³⁻¹⁷ Unlike Diodrast and neutral red, but like glucose, hemoglobin escapes only through the glomeruli; it is not taken from the blood and excreted by the tubule cells. Animals with no albuminuria show hemoglobinuria only when the plasma level exceeds 100 mg. per 100 cc. However, after prolonged hemoglobinuria, this threshold drops about 60 per cent. The actual leakage through the glomerulus represents only 2.5 to 3.0 per cent of the hemoglobin present in the plasma "cleared" of inulin in the same period. When the blood level is over 100 mg. per 100 cc., hemoglobin and hemosiderin appear in the cells of the proximal convoluted tubule and even farther along

in the nephron. Thus, reabsorption, threshold, and tubular storage and transformation occur with this protein, as they do with the carbohydrate dextrose.

Dawson,¹⁸ Hayman and Richards¹⁹ and Gérard,²⁰ with ingenious technics, introduced colloidal and particulate matter into the proximal end of the proximal convoluted tubule. They found these substances accumulated in visible masses in the cells of the tubules, proving that reabsorption and alteration in dispersion could occur with other substances than glucose and hemoglobin.

In our laboratory, Dr. E. Canat has recently performed some very instructive experiments using trypan blue and T 1824 (Evans's blue), both of which are adsorbed onto albumin, the Evans's blue very strongly. When 5 mg. of the latter dye is injected intraperitoneally in normal rats, no dye appears in the urine, and the proximal convoluted tubules show none after six hours and only very faint staining even after twenty-four hours. The dye is in small vacuoles, barely visible in unstained frozen sections and invisible if the ordinary eosin staining has been used. However, if rats with severe proteinuria (100 to 400 mg. a day) are given similar injections, the urine becomes intensely blue. As much as 0.7 mg. of dye may be excreted the first day, varying with the severity of the proteinuria—roughly 1 mg. of dye per 500 mg. of protein in the urine. But the tubules in the animal's kidney (only a small stump of one kidney remains in the experimental rat) show large, intensely blue granules of dye, and large numbers of such granules may be seen within six hours. The proximal convoluted tubule contains the most dye when the loss in the urine is most intense, but even when no dye escapes in the urine small amounts gradually appear in the tubules. This is interpreted to mean that small amounts of serum protein, with adsorbed dye, are constantly escaping into the glomerular filtrate and being reabsorbed by the tubules. The dye is concentrated in vacuoles after being split off from the protein, and faintly visible amounts occur in the normal animal after many hours. When proteinuria is present, large amounts of dyed protein leak out of the glomeruli, the tubular cells reabsorb large amounts but much escapes in the urine, large granules of dye, split off the protein and concentrated by the tubule cell, become visible in the cytoplasm in a few hours. The analogy with hemoglobin and with glucose is very close, for with these substances what accumulates in the tubules is a polymer or a split product of what was present in excess in the glomerular filtrate. The tubule not only reabsorbs but also "works over" these substances.

With Drs. Canat and L. G. Woolley, I have used Winton's technic (perfusion of kidneys with ice-cold serum) to obtain large quantities of glomerular filtrate. That the glomerular membrane is not damaged in successful experiments can be verified by the observation that hemoglobin added to the perfusate appears in concentrations only 2.5 to 3.0 per cent as great in the glomerular filtrate. In rabbits, the protein content of glomerular filtrate, obtained in volumes as high as 3 cc. a minute, when the tubules are paralyzed by cold, varies from 15 to 22 mg. per 100 cc. The glomerular filtrate thus obtained is water-clear with no tinge of yellow; it is, as Bickford and Winton²¹ showed, a pure ultrafiltrate with the glucose and chloride content of the plasma, and its protein content is about that of spinal fluid. Thus, the dye experiments receive confirmation regarding the probable presence of protein in the filtrate. It is hoped that this technic, applied to kidneys of animals with proteinuria and previously tested with hemoglobin, can give some information of the threshold level at which proteinuria occurs with a rise in protein content of glomerular filtrate.

It is well known that in the intense tubular damage due to severe hemoglobinuria or Bence-Jones proteinuria or with the crush syndrome (myoglobinuria), little or no fat appears in the tubules. In these cases, plasma lipids are normally low. In cases of Bright's disease with edema, with much fat in the tubules, plasma lipids are high, and this lipid is colloidal and often behaves as though adsorbed to globulin. The lipid is high when the albumin is low, suggesting that when the body can no longer supply colloidal protein to maintain oncotic pressure of the blood, it begins to mobilize colloidal fats. In any event, the blood is presumably the source of the fat that appears in the tubule cells, as it is of the iron in hemoglobinuria, the glycogen in diabetes and the Evans's blue in rats with severe proteinuria. Degenerative tubular changes, as Ekehorn⁷ and Govaerts^{22, 23} suggested, are not the cause but the result of fat and protein accumulation in the tubules. With proteinuria, the cortex of the kidney is swollen, hyaline and granular masses occur in the tubules, and desquamation (up to 100,000,000 epithelial cells a day in the sediment) follows this over-engorgement with reabsorbed materials. Such desquamation is easily repaired, as evidenced by the mitoses seen in these cases, and the tubular functions are scarcely altered. Cats normally have far more fat²⁴ in their tubules than is seen in the severest human nephrosis, and of course they too have excellent tubular function. Until the tubules are severely altered, as in anuric cases of hemoglobin or myoglobinemia,²⁵ the degenerative

change secondary to reabsorption leaves renal function almost intact. It is not impossible, however, that chronic proteinuria lowers the threshold at which protein leaks out of the body, and severe tubular changes may diminish capacity to reabsorb protein. In any event, the chief and the primary change is the rise in protein in the glomerular filtrate to levels at which tubular reabsorption no longer keeps pace with the supply. If the normal man has a threshold for spilling protein at 40 mg. per 100 cc., and normally has only 15 mg. per 100 cc. in the filtrate, he would have, in his 180 liters of filtrate a day, 27 gm. of protein, with none in the urine. At 41 mg., he would have 74 gm. in the filtrate and 2 gm. in the urine; if his threshold fell to 30 mg., with 41 in the filtrate, he would have 74 gm. in the filtrate and 20 gm. in the urine. These hypothetical figures give an idea of the way in which a slight rise in protein (or glucose or hemoglobin) in the filtrate can cause a huge increase in the urinary loss.

Proteinuria offers problems of diagnosis in medicine, pediatrics, surgery and obstetrics. Many types of investigation may be required to elucidate the cause in some cases, but no technic is more frequently of value than the quantitative study of the rate of loss of protein, cells and casts in the urine. Richard Bright set a bad example by sending his patients' blood and urine to Bostock, since in any field real skill is achieved only by those who thoroughly master and constantly employ the special technic necessary for study. It is as essential for the renal specialist to look at sediments obtained under standard conditions as for the heart specialist to do his own auscultation or the dermatologist to look at the entire skin surface.

There is evidence from the work in many laboratories on which to base an understanding of proteinuria and associated renal changes. This basis fits in with the knowledge of glycosuria and hemoglobinuria. But it leaves the central problem—the nature and cause of altered glomerular permeability—unanswered. More careful and constant scrutiny of patients and more ingenious and well-planned experiments will undoubtedly unravel much of this fundamental mystery.

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MEDICAL PROGRESS

REGIONAL ANESTHESIA

MANSON BROWN, M.D.,* AND MORRIS J. NICHOLSON, M.D.†

BOSTON

THE current progress of regional anesthesia is characterized by an interest in its military application, by increasing confidence in spinal and fractional spinal anesthesia, and by widening the use of block technics in the therapeutic field. Studies of anoxia, respiratory drive and vascular collapse have helped to rationalize the conduct of both spinal and general anesthesia.

Lahey¹ has pointed out that trained anesthetists in military service will contribute definitely to a lowered surgical mortality rate. In their hands, local anesthetics may be differentiated on the basis of effect on wound healing,^{2,3} fractures may be remobilized,⁴ and the use of spinal anesthesia will develop both in surgery and in the treatment of shock from injuries to the lower extremities.⁵

NEW AGENTS

Of the newer drugs available for regional anesthesia, monacaine hydrochloride,⁶ an isomer of procaine, holds some promise. Somewhat more toxic than procaine, it is more stable to room temperature and light and equally stable to sterilization, has a distinctly greater affinity for motor nerves, and is clinically reported to afford more lasting anesthesia.⁷

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*Formerly, fellow in Department of Anesthesia, Lahey Clinic, now, First Lieutenant, M.C., A.U.S.

†Member of the Department of Anesthesia, Lahey Clinic, anesthetist, New England Deaconess Hospital, associate anesthetist, New England Baptist Hospital.

Alkaline salts of procaine borate⁸ are less irritating than the commonly used hydrochloride, but deteriorate rapidly at room conditions. Potassium salts of procaine afford more lasting anesthesia, but are immoderately irritating.

Laboratory studies have suggested that Intracain⁹ might afford anesthesia twice as lasting as equivalent doses of procaine, but clinical trials have not confirmed this.

A group of piperidine derivatives¹⁰ has been studied and listed as PT-1, PT-4, PT-6, PT-14 and PT-19. Of these, PT-19 appears most promising, providing spinal anesthesia twice as lasting as procaine. In infiltration anesthesia, it is more toxic and less efficient than procaine. Clinical trial has not been reported.

Neothosol in almond oil¹¹ has been used without complication in 427 cases to secure prolonged anesthesia in abdominal wounds by infiltration during surgery. Research work on cats, with placement of this oil in healing wounds, revealed on microscopy little or no resulting reaction.

Isoamyl cupreine¹² (eucupin in oil and in Ringier's solution) has been utilized to infiltrate and to block operative wounds of the upper abdomen. Postoperative vital capacity is increased, and sequent analgesia (sometimes without anesthesia) decreases the patient's discomfort. Laboratory work suggests that accidental intrapleural injection of local agents in oil during nerve-block procedures may have no lasting ill effect.

THERAPEUTIC USES

The medical literature records an increasing use of local anesthesia in therapeutics. The antiseptic agent, rivanol,² combined with a local anesthetic, is suggested as an adjunct in the care of contaminated, painful wounds. This suggestion is timely, since local anesthetics derived from *p*-aminobenzoic acid (procaine) are antagonistic to the action of sulfonamide drugs when both are present in infected tissue.³ Local anesthetics in oil for prolonged anesthesia, or repeated paravertebral block of abdominal wounds, may decrease postoperative pulmonary complications. Regulated cell reception of a local agent in a slowly absorbable, non-toxic, gelatinous medium is claimed to have a similar effect.¹³

Local infiltration facilitates early mobilization in the treatment of fractures of nonweight-bearing bones and minor injuries,⁴ for example, those involving the back, shoulder, hand, wrist, ankle and foot.¹⁴ Fractured ribs may require only one or two injections for complete rehabilitation.¹⁵ Asthma and age are particular indications for such care. Anesthetic block is an adjunct to the treatment of fibrositis or bursitis,¹⁶ and offers temporary relief as well as frequently prolonged remission of neuritides, particularly the trigeminal, occipital, cervical, brachial, intercostal or sciatic types.¹⁷ Pain in amputation stumps may be interrupted or ended. Sympathalgia or causalgia of the face, traumatic "hard hand," or hyperhidrosis of the upper extremities may be improved by block of the stellate ganglion.

Articles by Bartlett¹⁸ and Seldon¹⁹ evaluate regional-nerve-block technics for surgery below the clavicles. Bilateral intercostal block is simple and serves admirably for plastic procedures on the upper abdominal wall, herniorrhaphy and closure of colostomy. Subtotal gastric resection in the patient who is a poor risk may be done readily under field block, with supplementary splanchnic block through the operative incision.^{20, 21} By this method, Finsterer²² reports good anesthesia in 90 per cent of 2442 cases; de Takats²³ reports success in 87 per cent of 1292 operations. General or fractional spinal anesthesia is needed for total gastric resection.

Tuohy,²⁴ of the Mayo Clinic, outlines excellent regional-block technics for saphenous ligation or femoral herniorrhaphy. He also describes procedures for caudal and transsacral blocks for anoperineal surgery and for work on the lower extremities.

Fetal and maternal risks are at a minimum under various types of caudal or, preferably, infiltration anesthesia.^{25, 26} Results under the latter are con-

sistent; perineal relaxation is notable, facilitating such procedures as low forceps, Scanzoni's maneuver, manual rotation, spontaneous breech and episiotomy. Anesthesia persists for one and a half to two hours.

The paravertebral sympathetic block for thrombophlebitis is an outstanding therapeutic application of regional anesthesia. All patients with superficial thrombophlebitis with pain and edema should have block and conservative measures.^{27, 28} In patients with deep phlebitis without lung infarction, those under forty years of age need sympathetic block and conservative measures. In those from fifty to seventy years of age, 7 per cent suffer pulmonary infarcts, and ligation with block should be done early. In patients over seventy years of age, 20 per cent are likely to have pulmonary infarcts; in this group, ligation is obligatory, and blocks may be palliative.²⁹ Ten cubic centimeters of 1 per cent novocain with epinephrine—1:200,000 at the first, second, third and fourth lumbar vertebrae—will give relief in ten minutes and marked improvement in an hour. Blocks should be repeated one or more times daily until the temperature levels. Lumbar paravertebral block will improve claudication if sympathectomy is indicated.³⁰ If done preoperatively, this procedure prevents ischemic gangrene after surgery on large arteries.³¹

Paravertebral dorsal procaine block eases pain in postoperative upper abdominal wounds and raises the postoperative vital capacity, which is usually between 20 and 40 per cent of normal, to 90 per cent of normal. This permits hyperventilation and cough, with less tendency to atelectasis.³²

Paravertebral alcohol injection may be preceded by diagnostic paravertebral cervicodorsal block for the relief of anginal pain or asthma.³³

X-ray studies of 2 per cent novocain in opaque oil show that in epidural anesthesia in human beings, the onset of anesthesia follows diffusion of the agent out along the nerve roots.³⁴ This method may be used caudally for sciatica, dorsally for relief of intractable pain in carcinoma, at about the seventh cervical to the second dorsal vertebra for angina or asthma, and at selected levels for thoracic surgery. In the thoracic field, spinal anesthesia is less desirable than epidural anesthesia, which does not diffuse to bulbar centers; the effect can be limited to a few spinal segments, the blood pressure fall, nausea and vomiting are less, and "puncture headache" is decreased.³⁵ A mixture of pontocaine and procaine may afford anesthesia for two hours or longer.³⁶ Some danger results if an accidental puncture of the dura is made, in view of the large amounts of agent commonly used (20 to 50 cc. of 2 per cent novocain).³⁷

SPINAL ANESTHESIA

Of the agents available for spinal anesthesia, procaine continues to be used most commonly; however, there is a tendency toward the use of solutions weighted with 6 to 10 per cent glucose to facilitate ready gravitation of the agent to desired sensory spinal levels.³⁸ In Britain, Percaine (nupercaine),³⁹ 1:200 with 6 per cent glucose, as well as pontocaine-glucose, is utilized; in this country, pontocaine hydrochloride, 1 per cent in 10 per cent glucose, is gaining popularity and has been used at the Lahey Clinic in about 8000 cases without a serious complication referable to the agent.

A significant contribution to subdiaphragmatic surgery during the last decade is the development of fractional (continuous) spinal anesthesia. This type, maintained with rubber tubing and an indwelling soft German-silver spinal needle, has now been used in a sufficient number of cases to permit evaluation.⁴⁰⁻⁴² It is particularly adapted to prolonged surgery in patients who are poor risks, in whom relaxation is desirable. The incidence of complications referable to the anesthesia is not greater than with any other comparable method.

Spinal anesthesia has been carried to cervical levels with some success, permitting such operations as mastoidectomy. On physiologic bases, this cannot be approved for it brings the agent perilously close to medullary centers, and depends on the selective paralysis of the sensory to the motor (phrenic) nerves.⁴³

Bourne,⁴⁴ who has modified the Etherington-Wilson technic for nupercaine to secure satisfactory spinal anesthesia for thoracic surgery, believes that with the use of this agent breathing is quieter, paradoxical breathing is decreased and secretions are less, and that the prolonged post-operative anesthesia aids convalescence. In these cases, intercostal or epidural block seems a more rational substitute for general anesthesia. Intratracheal cyclopropane or ether may be wholly preferable.

In the past, the fall in blood pressure experienced with spinal anesthesia was a barrier to its use for cesarean section. However, Heard⁴⁵ regards this disadvantage of spinal anesthesia as slight when the depressing effect of ether on the mother and fetus is considered. This bad effect of ether reaches its peak in abnormal fetuses or in heavy sedation of the mother. Circulatory, respiratory and genitourinary complications are reduced when spinal anesthesia is used, and the baby is not narcotized.⁴⁶

Hunt and Lundy⁴⁷ favor local or field block for cesarean section. To this technic, they have added

the intravenous administration of Pentothal Sodium when the uterus is opened because at that point some of their patients complained of distress. Oxygen or 50 per cent nitrous oxide and oxygen may be given for a few minutes if much Pentothal seems indicated.

CAUDAL ANESTHESIA . . .

Caudal anesthesia may also be utilized in parturition. Lahmann and Mietus⁴⁸ report 400 cases without incident, except a 2.5 per cent failure to produce anesthesia. Perineal relaxation occurs, contractions are painless, the uncontrolled "push urge" is diminished, separation and involution are normal, and the mother is rested. Continuous caudal anesthesia is also being used in obstetrics.⁴⁹

SUPPLEMENTARY ANESTHESIA

Premedication should be considered supplementary anesthesia, and is a vital factor in spinal anesthesia of any type. Pantopon in adequate doses, used instead of morphine, tends to decrease the incidence of nausea and vomiting.⁵⁰ Scopolamine is preferable to atropine, creating twice the drying effect and twice the psychic depression. The depressant effect of morphine, too, is more satisfactorily counteracted.⁵¹ When the drug is combined with Pantopon and a barbiturate if indicated, the exciting effect of scopolamine largely disappears.

Extensive surgery under spinal anesthesia may necessitate additional supplementary anesthesia, particularly if mesenteric traction initiates nausea and vomiting. The high concentration of oxygen that may be administered with cyclopropane is desirable but, in intra-abdominal surgery, may be contraindicated by the use of the cautery. In these cases, Pentothal Sodium administered by fractional doses into a continuous intravenous-drip apparatus is convenient. However, its depressing effect on the respiratory drive mechanism⁵² makes logical the simultaneous administration of nitrous oxide and oxygen, to prevent the patient from going into central respiratory failure.⁵³

SUPPORTIVE MEASURES

The value of an adequate oxygen supply to patients under prolonged spinal anesthesia with associated low blood pressure cannot be overemphasized. Arterial oxygen saturation, 5 to 45 per cent below normal in the head, can cause cerebral damage and a marked increase in water content (edema) of cerebral tissue.⁵⁴ This depression, added to the accepted histotoxic depression of Pentothal or preoperative barbiturates, helps to explain many of the accidents that have retarded the progress of spinal anesthesia.⁵⁵

The dangers of anoxia are inseparable from the problems of shock. Certain tests may detect shock during its earlier stages when significant changes are noted in the hematocrit, the specific gravities of the plasma and whole blood, and the plasma protein level.⁵⁶ The primary fall in blood pressure in spinal anesthesia probably depends on peripheral vasomotor paralysis. Other mechanisms accounting for the fall in blood pressure beyond the level caused by peripheral vasodilatation, suggested by Nowak and Downing,⁵⁷ are the central effects of vasomotor change and anoxia, in addition to medullary paralysis caused by direct extension and vascular absorption of the drug. When these tests or clinical observation indicate that shock is developing, electrolytes may be restored with physiologic saline, capillary tone with vasopressors and cortical extract, and the circulation sustained with blood or plasma.^{58, 59} Meanwhile, oxygen should be available, flowing in concentrations of about 60 to 75 per cent. Carbon dioxide should not be administered to spinally anesthetized animals or patients, since it lowers their blood pressure,⁶⁰ has little or no effect on respiration and contributes to already present anoxia.⁶¹

To combat the fall of blood pressure common with spinal anesthesia, ephedrine has proved to be the vasopressor of choice. As a working hypothesis, one may assume that spinal anesthesia blocks the sympathetics to the adrenals and lowers the epinephrine available. Then, if ephedrine is administered, it blocks amine oxidase, the epinephrine neutralizer, freeing "frozen" epinephrine. If ephedrine and fluids do not raise blood pressure and speed circulation, a small intravenous dose of epinephrine helps the depleted stores.⁶² A mixture of Pitressin and ephedrine elicits a more rapid and prolonged effect than ephedrine alone.⁶³ Too liberal administration of these pressor drugs may be somewhat dangerous in patients with arteriosclerosis or coronary disease. Epinephrine alone is efficacious, but its effect curve is too short and peaked.⁶⁴

An intermediate substitute for epinephrine is Synephrin tartrate.⁶⁵ A dose of 400 mg. secures a marked systolic rise, a slight diastolic rise and a slight fall in pulse rate. The onset is rapid, and the duration is over one hour.

Gaining favor is the related Neosynephrin, longer acting than ephedrine, and having less pressor and cardioirritant effect and more sympathetic side-effects.⁶⁶ The associated apnea sometimes observed is probably a carotid and aortic-body response to rapid elevation of blood pressure. The threshold doses are 2 mg. subcutaneously and 0.4 mg. intravenously; the average effective doses are 5 mg. subcutaneously and 0.8 mg. intravenously.

Overdosage creates cardiac irregularity and electrocardiographic variations.⁶⁷

Adrenocortical hormone (cortin) and desoxycorticosterone have been suggested as aids in the maintenance of blood pressure and in the treatment of shock. Desoxycorticosterone has no established value here. However, cortin has at least three uses: it protects against traumatic and adrenalectomy shock⁶⁸; under anoxic conditions, it is needed to mobilize catabolic protein and spare liver glycogen⁶⁹; and in the treatment of shock, it has a definite use in mobilization of fluids, particularly parenteral saline and plasma.⁷⁰

COMPLICATIONS

The complications arising under regional anesthesia are so varied as to prohibit an integrated discussion, but certain facts stand forth. Lyford⁷¹ reports that patients with normal respiratory systems before surgery have postoperative respiratory infections in about 6 per cent of cases; there is no relation to type of anesthesia. He states that patients with low-grade respiratory infection before surgery will have acute postoperative episodes two and a half times more frequently with spinal anesthesia than with inhalation anesthesia (spinal 39.5 per cent; ether 13.5 per cent; cyclopropane 17.5 per cent).⁷² These figures are not in accord with the very excellent work of King⁷³ at the Massachusetts General Hospital.

Postoperative atelectasis—much of the "ether pneumonia" of other days—has yielded well to catheter aspiration with conservative hyperventilation, together with limitation of sedatives. If this fails, therapeutic bronchoscopy is indicated, even in very sick patients, for pneumonia in a collapsed lung is far more inimical than bronchoscopy performed by fairly skilled persons.^{74, 75}

The prevention of atelectasis may be possible. Capelle⁷⁶ observed that the usual postoperative vital capacities of 20 to 40 per cent of normal were increased to 90 per cent of normal by continuous local anesthesia of abdominal wounds. Gius,³² impressed with Capelle's work, tried paravertebral intercostal block for atelectasis occurring after appendectomy in children, with notable success. Subsequent studies of vital capacities after abdominal surgery indicate that respiratory excursion, cough and movement are markedly facilitated by prolonged or repeated block anesthesia. Infiltrating such a wound at the end of an operation sometimes affords later analgesia without pinprick anesthesia.⁷² Starr and Gilman⁷⁷ report 23 per cent increase in postoperative vital capacity with blockage of the sixth to the tenth dorsal nerve inclusive.

The selection of cases (preoperative respiratory conditions) and of operations (nephrectomy and

cholecystectomy) for therapeutic intercostal block may markedly decrease the incidence of atelectasis. Few patients will object, for marked comfort is afforded.

The hypnotic drugs, such as Pentothal and Evipal, may create surgical or postoperative depression. At a deep anesthetic level (stage III, plane II), the cerebral respiratory centers may cease to function, and respiration becomes dependent on anoxic stimulation of the carotid sinus and aortic body. Carbon dioxide may pile up in the circulation until it actually interferes with oxygen transfer to tissues.⁶¹ At this point, a sudden supply of oxygen by mask may throw a patient into irreversible apnea.⁵² Such hypoxia is not well tolerated by patients under spinal anesthesia; therefore, hypnotics as supplemental anesthetics must be handled carefully. Postoperative hypnotic depression may be counteracted by benzedrine.⁷⁸ As yet, no relation between hypnotics and the toxicity of sulfonamides has been established.⁷⁹

Convulsions after bronchoscopy under topical pontocaine hydrochloride have been controlled by three 2-cc. doses of Dial.⁸⁰ Research suggests that in such cases calcium levulinate, calcium gluconate and calcium chloride are protective, in that order.⁸¹ Calcium chloride and Salyrgan protect against procaine convulsions, but only if injected with the anesthetic.⁸² Barbiturates given preoperatively protect, but increase the danger if injected with the anesthetic. Barbiturates used to excess for the control of cocaine convulsions cannot be counteracted as usual with Metrazol or picrotoxin; patients may have convulsions without awaking.⁸³

Further complications described in the literature are abducens paralysis, meningitis,⁸⁴ ventricular fibrillation, urinary retention and cauda-equina injury. Urinary retention, occurring in about 3 per cent of cases, usually responds to constant or tidal drainage with sulfonamide irrigations. Resection of a portion of the bladder sphincter has cured a refractory case.⁸⁵ Reported cauda-equina injury was seen in several patients given Spinocaine. Ferguson and Watkins⁸⁶ reported 14 such cases among seventeen hundred spinal anesthetics under durocaine, a procaine-gliadin-glycerine solution in 15 per cent-ethyl alcohol.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28431

PRESENTATION OF CASE

First admission. A fifty-eight-year-old man was admitted to the hospital because of a feeling of substernal oppression.

One year prior to admission the patient began to suffer with attacks of substernal oppression and chest tightness after exertion, without severe pain. These attacks were reduced in severity by rest and lessened activity. During the week prior to admission he suffered with almost daily attacks of "fluttering and bumping of the heart," each lasting about five minutes. During the attacks he had a feeling of impending danger; however, no remarkable pain developed.

The family history was noncontributory. Twenty-nine years previously the patient had had malaria, but since then he had had no chills. He did not recall having had any other tropical diseases.

Physical examination revealed a well-developed and well-nourished man in no apparent distress. The chest was of an emphysematous type but was otherwise normal. The heart when outlined by percussion was questionably slightly enlarged. The sounds were distant and faint. A blowing systolic murmur was audible at the apex. The abdominal examination was unremarkable, and no masses were felt.

The blood pressure was 120 systolic, 80 diastolic. The temperature was 99°F., the pulse 90, and the respirations 20. Several hours after admission the pulse was found to be 49, and during hospitalization it ranged between 50 and 60.

Examination of the blood revealed a red-cell count of 4,730,000 with a hemoglobin of 85 per cent, and a white-cell count of 10,800 with 68 per cent polymorphonuclears, 26 per cent lymphocytes and 6 per cent monocytes. The urine was normal except for a rare red cell and 2 white cells per high-power field in the sediment. The blood Hinton test was negative. The blood nonprotein nitrogen was 23 mg. per 100 cc. The sedimentation rate was reported 1 mm. in fifteen minutes, 4 mm. in thirty minutes, 6 mm. in forty-five minutes and 8 mm. in sixty minutes. An electrocardiogram demonstrated a normal sinus rhythm of 60 per minute. The P-R interval was 0.19 second; T₃ was inverted, and there was a slight amount of

left-axis deviation. The patient was discharged after three days and advised to take Nembutal at bedtime and 3 gr. of quinidine sulfate fifteen minutes before each meal.

Second admission (nine months later). The patient was readmitted because of a recurring fever of about 101°F., weakness and night sweats. These symptoms developed three months after discharge and seemed similar to the fever and chills with which he had suffered in the attack of malaria. A typical episode began at night with chills and trembling, followed by fever of 103°F., vomiting and sweating, which gradually decreased during the night leaving him weak but quite all right during the next day. Six weeks before entry he again began to have night sweats and evening fever, and these symptoms continued intermittently to the day of admission, being slightly mitigated by sulfadiazine administered by his local physician. Three weeks before entry his face became swollen and pink, and this skin flush gradually extended over the chest and abdomen and lasted several hours.

Physical examination was similar to that noted above except that the patient was obviously feverish. The soft systolic murmur was audible over the entire precordium, but best heard at the apex, and was transmitted into the left axilla.

The blood pressure was 110 systolic, 60 diastolic. The temperature was 101°F., the pulse 85, and the respirations 24.

Examination of the blood revealed a hemoglobin of 16.1 gm. and a white-cell count of 8000 with 75 per cent polymorphonuclears, 17 per cent lymphocytes, 7 per cent monocytes and 1 per cent blasts. The red blood cells appeared fairly normal; the platelets were slightly increased. No malaria parasites were seen. The urine examination was similar to that of the previous admission. A stool examination was negative for mucus and blood. Repeated examinations of the blood were not remarkably different, and no malaria parasites were found. Agglutination tests for undulant fever were negative, and the Widal test was negative. Repeated blood cultures revealed no growth.

An x-ray film of the chest demonstrated a small, rather sharply defined area of density in the right second interspace. There were areas of calcification in the right lower lung field, and linear scars in the left costophrenic angle. The heart was prominent in the region of the left ventricle. The aorta was tortuous. An electrocardiogram was similar to that taken during the previous admission.

During the nine days in the hospital, daily periods of fever up to 103°F. and sweating occurred in the evening, in spite of a brief course

of quinine sulfate. He was discharged with plans for readmission a week later. His fever had subsided somewhat.

Third admission (two weeks later). Since discharge he had had a gradual return of pyrexia, although for the first week at home his temperature was subnormal.

The physical examination had not changed except that the patient was definitely sicker.

The temperature was 101.4°F., the pulse 89, and the respirations 20.

The hemoglobin level was 10.3 gm., and the white-cell count 9200 with 64 per cent polymorphonuclears, 17 per cent lymphocytes and 19 per cent monocytes. No malaria parasites were seen in the blood smear. The urine examination was unchanged except for a + test for albumin. An electrocardiogram did not demonstrate any remarkable change. An x-ray film of the chest showed some hazy density extending upward and posteriorly from the right hilus, apparently in the apex of the right lower lobe.

The patient was discharged after six days without much improvement.

Final admission (two weeks later). Since discharge, he had had a subnormal temperature for one week and then it gradually rose from an evening peak of 99°F. on the first day of the week to 104°F. on admission, with profuse night sweats and daily remissions. He had been taking 40 to 80 gr. of aspirin each day and had recently developed some deafness and ringing in the ears. Three or four days before entry he noted the onset of attacks of rapid pulse, which often rose from 78 to more than 150. These changes occurred suddenly, lasted a few minutes and stopped suddenly. He had had twenty to twenty-five attacks during the four days prior to admission. They were accompanied by a burning headache and perspiration. All these symptoms ceased with cessation of the rapid pulse rate. There was no dyspnea or precordial distress with the attacks.

Physical examination revealed a flushed, apprehensive man with a hot, dry skin, who looked chronically, but not acutely, ill. The examination of the lungs was normal, except for equivocal dullness at both bases posteriorly and a suggestion of bronchovesicular breathing in these areas. A few fine rales were audible at both bases. The heart was markedly enlarged to the left in the anterior axillary line, and the apex impulse was felt in the left fourth interspace in the anterior axillary line. There was a moderately loud blowing systolic murmur over the entire precordium which was best heard at the apex and was transmitted to the left axilla. A somewhat rasping but soft systolic murmur was audible at the base and in the neck vessels. Along the left border of

the sternum there was a midsystolic scratching sound, which seemed more like a precordial rub than transmission of a systolic murmur.

The blood pressure was 134 systolic, 74 diastolic. The temperature was 104°F., the pulse 90, and the respirations 32.

Examination of the blood revealed a hemoglobin of 9.7 gm. and a white-cell count of 5600 with 86 per cent polymorphonuclears, 10 per cent lymphocytes, 2 per cent monocytes and 2 per cent myeloblasts. The urine was unchanged, as was an x-ray film of the chest. In the flat plate of the abdomen the kidney shadows were obscured by overlying bowel but were not grossly abnormal. There was a small area of density overlying the right side of the sacrum. Further blood cultures revealed either no growth or obvious contaminants. The urine culture was negative. A stool examination was negative for blood, mucus, amebae and amebic cysts. An intravenous pyelogram was negative. A cephalin flocculation test was +++ at 24° C. and ++++ at 48° C., but in the liver-function test there was less than 5 per cent of the dye in the serum. One month after admission, tiny lymph nodes about 5 mm. in diameter, were felt in the neck on each side.

Since no diagnosis was established, the patient was empirically treated with a course of sulfadiazine by mouth, totaling 69 gm. in seventeen days. The blood level established apparently did not exceed 5.9 mg. per 100 cc. There was only a moderate reduction in the temperature during the course of sulfadiazine, and the patient was not remarkably improved. His fever continued to spike to 103 or 104°F. almost every day. Short courses of quinine sulfate and Atabrine were administered without obvious improvement. In spite of supportive and symptomatic treatment, the patient gradually became weaker. In the last week before death, three small lymph nodes became palpable for the first time in the groins, and the patient gradually became moderately jaundiced. Symptoms of fever and chills continued, and the patient died three months after admission.

DIFFERENTIAL DIAGNOSIS

DR. FRANCIS R. DIEUAIDE: In reading through the abstract, we note that the first complaints were those of anginoid attacks with runs of premature beats, that is, short attacks of paroxysmal tachycardia or possibly, though less likely, paroxysmal auricular fibrillation. These were repeated during the fourth admission. The mid-diastolic scratching sound along the left border of the sternum leads me to believe that the patient had a mild pericarditis at the time of the fourth admis-

sion. The blood pressure showed changes up and down, which were not, however, very great.

The blood changes include the finding of 19 per cent monocytes and 1 per cent myeloblasts on different occasions. It is not safe to attribute great importance to these. By the time of the last admission there was moderately severe anemia. The whole course of the patient, if we consider the beginning to be when he first had substernal discomfort, took about two years. The chills and fever lasted about ten months. These recurrent attacks of fever are very striking and must contain the central clue to the diagnosis. Apart from them, the findings point in three directions.

Certain findings relate to the heart. We know that the patient had substernal discomfort. He had paroxysmal attacks of tachycardia, with some variation in blood pressure, and developed marked enlargement of the heart to the left, with a loud systolic murmur. He apparently never developed congestive failure, had no sign of valvular disease and, during observation, had no hypertension. He probably had a short episode of acute pericarditis during the last admission. There is no reason to think he had a huge pericardial effusion as a possible explanation of the apparent enlargement of the heart.

Another direction in which our attention is drawn is the liver, since we are told that the patient had jaundice.

The third direction we must consider is suggested by the lymph glands in the neck and in the groin, which were small and apparently did not attract much attention. There were also some findings in the chest.

May we see the chest films, please?

DR. GEORGE W. HOLMES: The shadows spoken of in the chest are these small spots of calcification. I should not say that they had any particular bearing on this patient's story.

There is a moderate amount of tortuosity of the aorta, and the heart seems to extend a little farther to the left than usual, but in view of these other things I doubt if it is actually enlarged. The left ventricle is perhaps a bit prominent. The other things that were mentioned I think are of no importance. These lines are probably blood vessels; there is nothing characteristic about them.

DR. DIEUAIDE: Do you think anything of that shadow at the right hilus?

DR. HOLMES: No; one might say the pulmonary vessels are a little prominent. I do not believe that would be of any aid in the diagnosis or that one was justified in saying it was definitely abnormal.

DR. DIEUAIDE: I am very humble about this, but is that not a well-defined outline at the hilus—more so than usual?

DR. HOLMES: I do not believe so. I should not call it abnormal, much as I should like to agree with you. There is one strange thing about this. At one time his heart was said to have been enormously enlarged. I do not see any evidence of it in any of the films. If he did have enlargement, it apparently disappeared.

One would like to try to find out something about the size of the liver though these films were not taken for that purpose. It is not enlarged; if anything, it is small. Also you can see the outline of the spleen, and that does not seem enlarged. The kidney shadows are large as we see them on the film but no larger than a heavy man should have. They are magnified a good deal.

I am afraid most of my evidence is negative.

DR. DIEUAIDE: If we depart for a moment from this point and think about the febrile course, which is the most striking aspect of the case, we must run over a number of possibilities. In the first place there are many varieties of low-grade septicemia, including bacterial endocarditis, brucellosis and many other infections. This patient had a normal white-cell count, which is against many of these infections, but is not exclusive. He had no enlargement of the spleen, so far as we know, and no embolic phenomena (petechiae, subcutaneous nodules, nephritis, and cerebral or pulmonary embolism). He had no valvular disease of the heart, which puts out bacterial endocarditis. He had many negative blood cultures, which in the end one has to take as being against septicemia.

One should always consider tuberculosis. This man was fifty-eight years old; it is the fashion to think that people as old as that do not get tuberculosis and die of it, but this is a mistake—they do. On the other hand, in ten months, tuberculosis should declare itself in the chest, abdomen or meninges, unless one is dealing with some peculiar localization, such as the adrenal glands, of which there is no indication. Tuberculosis is not out of the question, but I do not believe it is the diagnosis.

Typhoid fever is always mentioned in these cases. Again, in ten months it should be picked up, and I think we can throw out the possibility.

Is this malaria after twenty-nine years, without any remissions after quinine, without any enlargement of the spleen and with death? No, I do not think the patient had malaria.

A new growth, such as lymphoma, has to be one of the possibilities that we think of seriously. Such a patient would be studied thoroughly for some localization of the tumor, and I assume that this was done. Could these little lymph nodes be the only signs of new growth? Could this shadow

in the chest be a mass of lymph nodes and be more significant than hilar vascular changes? In this large group of possibilities cannot be left out.

Next, we must consider hepatic disease. The patient undoubtedly had some form of liver disturbance, since he had progressive jaundice. The abstract gives only the results of liver function tests and does not mention palpability of the organ. Perhaps we may assume that it was not palpable. The flocculation test was positive, but the bromsulfalein test gave normal results. It might be of interest to know whether there was a long interval between the bromsulfalein test and death.

DR TRACY B. MALLORY: There was a three month interval.

DR DIEUVIDE: In other words, the bromsulfalein test was done at the beginning of the third admission, and therefore it does not do what we should like it to do. If the patient had diffuse liver disease at the time of death, I am sure that the bromsulfalein test would not have been normal at the end. With serious disease of the liver as the fundamental cause of death, we should expect a declaration of the disease in a well observed patient in the form of jaundice, ascites, liver enlargement, pain about the liver and evidence of hepatic insufficiency. Of these only jaundice appears. I do not believe that hepatic disease was the cause of death.

Phlebitis might be mentioned, but there is no lead to that—no localizing signs and no evidence of embolism.

Then, there are certain obscure diseases that have to be brought up. I suppose there are many others, but there are three which especially come to mind. disseminated lupus, sarcoid and periarteritis nodosa. So far as disseminated lupus and sarcoid are concerned, we have not the vaguest clinical suggestion that either of these conditions would have been found post mortem. Periarteritis nodosa could be the diagnosis, although there is a question whether patients have been seen with such fever as this. I hope someone else will speak about this point before we know the diagnosis. So far as I know, the febrile episodes are out of line with this possibility, but many of the other findings are not. In the first place, some of the cardiac events would fit in—the anginous syndrome, with the substernal oppression, the variation in the blood pressure and even cardiac enlargement and pericarditis; the age and duration of the disease are compatible. The patient did not have the outstanding characteristic features of periarteritis, such as leukocytosis, eosinophilia, abdominal pain, nodules, enlargement of the

spleen and so forth. However, all these findings are seen in only a very moderate percentage of patients with periarteritis nodosa.

As Dr. Mallory anticipated, I am unable to make a definite diagnosis. I am going to make periarteritis nodosa my first choice and put down neoplasm, perhaps lymphoma, in the next line.

CLINICAL DIAGNOSIS

Hodgkin's disease?

DR DIEUVIDE'S DIAGNOSIS

Periarteritis nodosa?

New growth (possibly lymphoma)?

ANATOMICAL DIAGNOSES

Malignant lymphoma, Hodgkin's sarcoma type, involving lymph nodes, spleen and bone marrow.

Icterus

Central necrosis of liver.

Atherosclerosis moderate aortic, coronary and pulmonary.

Emphysema, moderate.

Cholelithiasis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This was obviously a most obscure case. At autopsy, we found several very slightly enlarged lymph nodes, a perfectly normal liver and a slightly enlarged spleen without any characteristic markings or nodules. It seemed to me impossible to make any diagnosis on the gross findings. When the microscopic sections came through, it was obvious that these not very important looking nodes all showed typical Hodgkin's disease, that there were many scattered Sternberg cells in the unimpressive spleen and that the major Hodgkin's disease was in the bone marrow, which was almost 75 per cent replaced by the disease. The heart was normal in size, and there was only 80 cc. of pericardial fluid. There was nothing to indicate that there had ever been a pericarditis. There was moderate emphysema.

A PHYSICIAN: Was there a mediastinal mass?

DR. MALLORY: There was very slight enlargement of the hilar glands, but no mass.

DR. DIEUVIDE: Did they show Hodgkin's disease?

DR. MALLORY: Yes.

CASE 28432

PRESENTATION OF CASE

A thirty-two year old man was referred to the hospital because of fever, chills, diarrhea and jaundice.

Three weeks prior to admission he noticed extreme weakness on arising in the morning. He went to work but was forced to return home in the afternoon because of extreme weakness and fatigue. Because he did not feel up to par, he took a laxative, which produced watery stools for two days. At no time was blood noticed in the stools. He was seen on the following day by his physician, who told him that his temperature was 102°F. He was urged to enter a hospital, but he postponed this for four days, during which period he had several chills and suffered with vague poorly defined abdominal pains largely confined to the epigastrium but not well localized.

On admission to a community hospital he was very dehydrated and prostrated, obviously quite ill. He was treated with sulfathiazole, apparently by mouth and, after 45 gr. of the drug had been given, was found to be jaundiced. For this reason the drug was discontinued. Laboratory studies revealed a red-cell count of 4,200,000 with 80 per cent hemoglobin, and a white-cell count of 6000 with 90 per cent polymorphonuclears. Two blood cultures were reported negative. A test for Weil's disease done at a federal laboratory was reported negative. Repeated Widal tests were negative. The urine was negative except for a rare red blood cell, an occasional granular cast and many bacteria. The stool examination revealed only a ++ guaiac test. The stools did not contain gross blood and were not tarry. The van den Bergh test and icteric index were first reported 10.7 mg. per 100 cc. and 13, respectively, and when repeated several days later, were 5.27 mg., and 6.7. During the two weeks in the hospital he became progressively anemic and the white-cell count rose to 12,000. He became progressively worse, the illness being characterized by weakness, chills and evening temperature elevations to 106.8°F., with a morning temperature of 100°F. At times he complained of a slight pain localized in the upper abdomen. Bowel movements were regular, but the stools seemed to be lighter in color than normal. There were no urinary symptoms. Because no diagnosis could be established, he was transferred to another hospital for further study. Here the picture remained essentially as previously noted except that a blood culture demonstrated gram-positive cocci in short chains and many diplococci. When cultures were repeated, no cocci were found but many large gram-positive (*sic*) rods were cultured, which proved to be Friedländer's bacilli. X-ray films of the abdomen demonstrated a dense somewhat homogeneous soft-tissue mass, which filled the entire epigastrium. There was an irregular fleck of calcium to the left of the third lumbar interspace, which was thought to

have no connection with the soft-tissue shadow. The liver and spleen appeared moderately enlarged. The shadows of the kidneys and psoas muscles were distinctly seen. The gas-filled transverse colon was depressed and lay just above the pelvis. Re-examination of the abdomen with a swallow of barium outlined the stomach, which was flattened and displaced to the left and downward by the previously noted round soft-tissue mass. There was no obstruction. There was no definite evidence of intrinsic disease of the stomach, and the duodenal loop was small. The patient was started on sulfadiazine, and after eighteen hours, the blood level was 7.1 mg. per 100 cc. He had three chills during the two days' stay at the hospital, and the temperature fluctuated between 100 and 104°F. He had no specific complaints other than weakness, chills and fever. No diagnosis was established. The patient was brought to this hospital for further study and care.

The family history was not contributory. The patient lived in the country and was accustomed to drinking well water, which he obtained from his own well. This was said to be 18 feet deep, and the water was declared good. He used a privy. He stated that he had always used raw milk until three weeks prior to the present illness, when he changed to condensed milk since raw milk was difficult to obtain. He had never been immunized against typhoid fever and had been unsuccessfully vaccinated against smallpox. He smoked occasionally and did not use alcohol excessively. Ten years previously, when admitted to a government hospital for a circumcision, a scar was found on the glans penis. He denied having had a penile sore or having had gonorrhea. Serologic tests at that time were negative for syphilis.

Physical examination revealed a feverish, jaundiced young man perspiring profusely and obviously acutely ill. Examination of the lungs and heart was negative, except for a soft apical systolic murmur. The abdomen was moderately distended and tympanitic. No masses were palpable, and the liver edge could not be percussed because of abdominal tympany. The upper border of liver dullness seemed elevated, and the area of splenic dullness was increased. There was slight tenderness in the right upper and right lower quadrants. Normal peristaltic sounds were audible. The rectal examination was negative.

The blood pressure was 125 systolic, 84 diastolic. The temperature was 102.4°F., the pulse 99, and the respirations 24.

The examination of the blood revealed a red-cell count of 2,410,000 with a hemoglobin of 50 per cent and a hematocrit of 25 per cent, and a white-cell count of 17,100 with 91 per cent polymorpho-

nuclears. The urine was acid in reaction, had a specific gravity of 1.018 and showed a $+$ test for albumin. The van den Bergh was 2.5 mg. per 100 cc., and the chloride 96.9 milliequiv. per liter. The prothrombin time was 25 seconds (normal, 20 seconds), the protein 6.1 gm., the blood sugar 94 mg. and the nonprotein nitrogen 23 mg. per 100 cc., and the bicarbonate 20.0 milliequiv. per liter. A flat plate of the abdomen demonstrated barium scattered throughout the colon, with a portion of it in the rectum. The psoas shadows were slightly indistinct. The kidneys were faintly seen. There was increased haziness throughout the upper abdomen, but no definite mass was seen. The splenic flexion of the colon was definitely lower than normal.

A course of sulfadiazine was started, and a transfusion of citrated blood was administered. The second day after admission, the patient was operated on.

DIFFERENTIAL DIAGNOSIS

DR. ALLEN G. BRAILEY: In striving to unravel this story, we might begin by asking what was the nature of the disease that made this patient ill, and it seems obvious that it was acute infection. Then we might ask in what organ or system the infection had a primary focus, and there again it seems obvious that it had to do with the biliary tree. An illness that is characterized by extreme weakness, chills, fever and the development of jaundice and anemia might well be due to pylephlebitis. The commonest source of such a pylephlebitis is the appendix. The organisms enter the portal vein and cause septic thrombi and then emboli, which lodge here and there throughout the liver and result in the production of multiple abscesses. Appendicitis may occasionally produce very few symptoms, but in this case there is no hint whatever of antecedent appendiceal infection unless one wants to attach importance to the fact that there was tenderness in the right lower quadrant. I feel hesitant about making a diagnosis of appendicitis on such slender evidence as that. Of course, pylephlebitis might rarely originate from infection elsewhere in the gastrointestinal tract. There is the note of a positive guaiac test from one hospital, so that a certain amount of occult blood had been present. I should think there were adequate reasons for that amount of blood in an inflammatory process in the biliary tree and areas surrounding the duodenum, but I suppose he might have had a small ulcer somewhere in the gut, which initiated a pylephlebitis.

Then, there is acute suppurative cholangitis, which is an interesting disease and is sometimes secondary to infection elsewhere, such as pneu-

monia, influenza or, occasionally, typhoid fever. Most commonly it follows cholecystitis. When it originates primarily in the biliary tree, it usually follows obstruction of the biliary tract, such as that from stone, tumor or echinococcal cyst or, occasionally, from intestinal worms, which may obstruct the common duct. When it is due to biliary obstruction one expects to find the biliary tree widely dilated and filled with pus. The walls are thickened, there are multiple small periportal abscesses, and the history is quite like this, with extreme weakness, a spiking septic temperature, the gradual development of jaundice and, usually, a fairly rapid fatal termination. No obstruction to the biliary tree is necessary, however; it may develop as a result of a blood-borne infection originating elsewhere or, sometimes, de novo. The organisms involved are usually streptococcus, *Staphylococcus aureus*, pneumococcus and others. I am somewhat dismayed by the bacteriologic situation. Four blood cultures were taken. Two were negative. One showed gram-positive cocci in short chains and diplococci, which I should guess were contaminants. Then one showed gram-positive bacilli that were said to be Friedländer's bacilli. This bacillus is a gram-negative, encapsulated organism, also known as *Bacillus mucosus capsulatus*, and is responsible for 5 to 7 per cent of pneumonias, which are highly fatal and characterized, among other things, by sticky tenacious sputum. It is also an interesting organism in that it is closely related to the colon group and can at times be isolated from intestinal contents. It may give rise to infection of the intestinal tract and of associated organs. I do not know that any great importance need be attached to this report of Friedländer's bacillus; but still, if it was found, it probably indicates a bacteremia. Perhaps the infectious process was due to that organism.

Now let us consider this epigastric mass of which we have this account that is so indefinite. It might, of course, have been a tumor, a lymphoma or another mass, that served as the cause of the obstruction of the biliary tract. It might also have been an extrahepatic abscess. Abscesses within the liver not infrequently, or at least occasionally, rupture through the capsule and produce such a mass. The associated infection of the common duct and gall bladder might have done likewise. Of course, if there were such an extrahepatic abscess that developed slowly enough it would have been walled off by the omentum and localized to the upper abdomen.

I do not know what this man had. On the whole, I think he had an acute suppurative cholangitis; whether this was initiated by pylephlebitis I do not know. I do not believe the surgeons knew

either. I think he was probably operated on with the idea of draining the obvious septic focus, either in the biliary tree or an extrahepatic abscess.

DR. RICHARD H. SWEET: Would it be fair to make a comment from a clinical standpoint on the description of the mass?

DR. TRACY B. MALLORY: Yes.

DR. SWEET: There was a mass. I thought that it was liver. It felt like a mass within the liver in the epigastric region and was not tender.

DR. BRAILEY: Then it might have been an intrahepatic abscess that deformed the normal liver margin. I doubt if an abscess of the liver would of itself be of sufficient size ordinarily to be palpable in the epigastrium. Do you think it might have?

DR. SWEET: Yes, it might.

DR. BRAILEY: Then perhaps the mass was all inside the liver.

DR. MALLORY: Then your preference is cholangitis with multiple abscesses in the liver?

DR. BRAILEY: I will stick to that.

DR. MALLORY: Does anyone else care to express a preference?

DR. REED HARWOOD: I think the possibility of Weil's disease should be mentioned in the list of diagnoses.

DR. MALLORY: That was thought of and serum for an agglutination test was sent to Washington; the report was negative.

DR. SWEET: If my recollection of this case is correct, the surgeon did make a diagnosis in spite of what Dr. Brailey has said. It was based largely on the history and the finding of the mass. I thought he had an abscess of the liver, and I therefore made an incision directly over the mass and found it was in the liver, chiefly in the left lobe. I aspirated it with a long needle and discovered a deep-seated abscess. It has been pointed out that liver abscesses are tender and it has been said that if one operates under local anesthesia the exact location of the abscess can be identified by palpation. We have tried that here and have found that most of the liver abscesses are not tender until they present near the surface and set up local peritonitis or pleuritis on the diaphragmatic surface. We drained the abscess, but it was obvious to me even at that time that there were many others. I could feel several suspicious spots throughout the liver.

It was my opinion that the thing started from his appendix. Whether I was influenced by the common history of appendicitis as a seat of the source, I cannot say.

DR. BRAILEY: Would not a more careful history have revealed something?

DR. SWEET: As a matter of fact, he was gone over with a great deal of care in an excellent

clinic here in Boston, where the history and examination are notoriously thorough and complete, and they did not make a diagnosis of appendicitis. He was seen by one of our surgeons at that clinic, and he did not make a diagnosis. We questioned the patient at length and thought that there was something going on in the abdomen, with the chills and fever. In a young man who subsequently had some sort of inflammatory reaction in the liver we believed that the most likely source was the appendix. By the time he was first seen, however, the process was obviously beyond the point where an operation on the appendix would have been of any use.

CLINICAL DIAGNOSIS

Liver abscess.

DR. BRAILEY'S DIAGNOSES

Acute suppurative cholangitis.

Pylephlebitis?

ANATOMICAL DIAGNOSES

Appendicitis, acute gangrenous, with rupture into root of mesentery.

Appendiceal abscess.

Pylephlebitis, suppurative: ileocolic and portal veins.

Hepatic abscesses, multiple.

Jaundice.

Splenitis, toxic.

Thrombosis of splenic vein.

Operative wound: drainage of hepatic abscess.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At autopsy we found a liver filled with abscesses. On making a nick in the portal vein, pus welled from it, and then on pressing any spot in the liver more pus could be squeezed out of the portal vein, making it clear that all the multiple abscesses in the liver communicated with the portal system. Tracing down the portal radicles, we found the ileocolic vein likewise filled with pus. In the right lower quadrant was a localized peritoneal abscess, and projecting into that was the stump of an appendix from which the tip had blown off.

The liver weighed 2600 gm., and the spleen 800 gm., so that there was a lot of tissue in the upper abdomen. It is not surprising that the x-rays did not penetrate very well in that region. Our post-mortem cultures from these abscesses showed only colon bacilli and streptococci. We were unable to confirm the report of Friedländer's bacillus, which would, I think, be a very unlikely organism to find secondary to a perforated appendix.

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COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fowey, Boston, Massachusetts.

INSTITUTE ON INDUSTRIAL MEDICINE

EVERY registered physician in Massachusetts has received a copy of the program of the postgraduate institute, "Industrial Problems in Medical Practice," to be held at the Harvard Club, 374 Commonwealth Avenue, Boston, on Saturday, November 7, under the auspices of the Committee on Postgraduate Instruction and the Committee on Industrial Health, Massachusetts Medical Society, in co-operation with the Massachusetts Department of Public Health and the Division of Occupational Hygiene, Massachusetts Department of Labor and Industries.

This attractive all-day program by authoritative speakers, which appears elsewhere in this issue of

the *Journal*, should appeal to every practicing physician, particularly in view of the fact that industrial medicine, in one or another of its many ramifications, is of paramount importance to the continuation of the war effort and a topic with which the majority of physicians are unfamiliar.

Luncheon and dinner will be served at the Harvard Club, but those who plan to attend these functions should signify their intentions in advance, since the seating and serving facilities are limited. Dr. George Leonard Schadt, president of the Society, will preside at the dinner, which will be followed by two serious but entertaining speakers. Because of the timeliness of the subject to be discussed at this meeting, all physicians are urged to attend.

NATIONAL HEARING WEEK

DEAFNESS is a national ill, and now that another war is in process, those so afflicted will increase in alarming numbers. Among the hazards to which the hearing organ may be exposed are excessive noise, gunfire, direct injury and barometric influence. Consequently, there probably has never been a time when both physicians and the laity need to be made more aware of the organized efforts that are being made for the prevention and amelioration of deafness.

The American Society for the Hard of Hearing and its one hundred and twenty-one local affiliates in the United States and Canada have done a great deal to educate and to bring about co-operation among the public, members of the medical profession and the hard of hearing. Among other things, it has accomplished a notable piece of work in fostering hearing tests and promoting lip reading in the public schools, in investigating hearing aids and advertised "cures" and in encouraging research in the medical control of deafness. The society also promotes adult lip reading, social service and vocational opportunities for the hard of hearing everywhere, thus acting as a unifying force to make life easier and better for those so afflicted.

The Boston Guild for the Hard of Hearing, the local chapter, is uniting in the nation-wide observance of National Hearing Week, October 25 to 31. This period will be devoted to the education of the public in the problems of the hard of hearing and to the demonstration of the many facilities that are provided. Because this annual event, held at the headquarters at 283 Commonwealth Avenue, is of so much value to the population as a whole, three papers in this issue of the *Journal* are devoted to the subject of hearing health. Both otologists and general practitioners should give their hearty endorsement to this constructive service for the hard of hearing.

MEDICAL EPONYM

SAHLI HEMOMETER

The hemometer was first described by Professor Herman Sahli (1856-1933), of Bern, in a paper, entitled "Über ein einfaches und exactes Verfahren der klinischen Hämmetrie [A Simple and Exact Method of Clinical Hemometry]," which was read at the Twentieth Congress for Internal Medicine in April, 1902. The article appeared in *Verhandlungen des Congresses für Innere Medizin* (20:230-234, 1902). A portion of the translation follows:

After numerous attempts, I have succeeded in finding a method of converting the hemoglobin in a solution of blood into a derivative, by means of a very simple reaction, whereby stable standard solutions can be prepared and colorimetric determinations carried out. . . . The method consists simply in adding to the blood ten times the amount of one-tenth normal hydrochloric acid. After a few seconds, the solution turns deep brown and becomes a clear, brownish yellow after dilution with ordinary water. The pigment content may be colorimetrically determined by means of a similar standard solution, which can be so made as to be completely stable.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEES ON POSTGRADUATE INSTRUCTION AND INDUSTRIAL HEALTH

The program for the postgraduate institute, "Industrial Problems in Medical Practice," to be held at the Harvard Club, 374 Commonwealth

Avenue, Boston, on Saturday, November 7, is as follows:

Morning Session

Presiding Chairmen: Dr. Dwight O'Hara
Dr. Reginald Fitz

- 8:30 *Registration.*
- 9:15 *Opening Remarks.*
- 9:30 *The Value of Pre-employment Examinations.* Dr. Daniel L. Lynch.
- 9:45 *The Personality of Industrial Applicants.* Commander A. Warren Stearns, M.C., U.S.N.R.
- 10:00 *Toxic Fumes and Gases in Industry.* Dr. Alan R. Moritz.
- 10:45 *Industrial Dermatitis.* Dr. John G. Downing.
- 11:15 *Question Period.*
- 11:30 *Round-Table Discussion on the Treatment of Burns.* Drs. Edward D. Churchill, S. Howard Armstrong, Oliver Cope and Charles C. Lund.
- 12:45 *Luncheon.*

Afternoon Session

Presiding Chairmen: Dr. Bennett F. Avery
Dr. C. Sidney Burwell

- 2:00 *Injuries to the Eyes.* Lt. Commander Edwin B. Dunphy, M.C., U.S.N.R.
- 2:30 *Examination and Diagnosis of Lane-Back Conditions.* Dr. Frank R. Ober.
- 3:15 *Recess.*
- 3:30 *Round-Table Discussion on the Modern Treatment of Wounds.* Drs. Champ Lyons, Henry C. Marble, Joseph H. Shortell and Gordon M. Morrison.

Evening Session

Presiding Chairman: Dr. George Leonard Schadt

- 6:30 *Dinner.*
- Responsibility of Physicians to Industry in Winning the War.* Lt. Colonel Anthony J. Lanza, M.C., U.S.A.
- Sterilization in Operating Rooms.* Dr. Carl W. Walter.

REGINALD FITZ, *Chairman*
Committee on Postgraduate Instruction

DWIGHT O'HARA, *Chairman*
Committee on Industrial Health

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH
IN MASSACHUSETTS DURING 1941

SEPSIS

The tabulation printed in last week's issue of the *Journal* showed that 243 puerperal deaths occurred in Massachusetts during 1941 and that, of these, 48 patients died of sepsis. In the septic

cases, 22 were associated with abortion, of which 13 were medicolegal. It is impossible to say how many of these were criminal abortions, but there was only 1 case that might have been associated with a spontaneous abortion. There were 3 cases in which drugs were said to have been the causative factors, although there is no pharmacologic basis for the assumption that drugs play a part in abortions. Thirteen autopsies were performed, and 7 of these were in cases that followed septic abortions, 2 of which were proved to have been associated with gas-bacillus infection.

These 22 septic cases following abortion illustrate the seriousness of attempting to interfere with a normal pregnancy; and the figures, of course, do not include the far greater number of patients who, following an abortion, developed pelvic sepsis with invalidism and, oftentimes, sterility, which not infrequently demanded hysterectomy. A frank discussion of the dangers of abortion is the only way in which to bring the seriousness of this problem to the laity. Of course, all these deaths are preventable.

Of the other 26 cases allocated to sepsis, 6 were associated with normal delivery. One of these may have been caused by alveolar abscesses that were surgically drained. There was not enough evidence to comment on the value of chemotherapy in such cases.

It is gratifying to find that only 3 septic cases were associated with operative vaginal deliveries. Two patients were delivered by low forceps: in one case, sepsis developed immediately after delivery and an autopsy showed that peritonitis had been caused by a rupture of the lower uterine segment, and the other patient developed a fever on the third day after delivery and in spite of apparently intelligent chemotherapy succumbed nineteen days later. The third case in this group was a patient, six and a half months pregnant, in whom a cicatricial cervix made normal dilatation impossible; insertion of a Voorhees bag was attempted unsuccessfully, and sepsis developed intra partum; delivery was consummated by a vaginal cesarean section, and the patient died a few hours later.

Fifteen septic cases were delivered by cesarean section. Of these, 3 had the benefit of autopsy: in two, the diagnosis of peritonitis was confirmed, and in the third, adynamic ileus was apparently the cause of death, without sepsis being the underlying factor. One section was done because of a placenta previa. There were 3 cases in which cesarean sections had been previously performed. The first patient, who had had acute heart failure and chronic bronchitis associated with myocarditis in 1931, was given spinal anesthesia to prevent

inhalation irritation; however, sepsis developed. Another patient had no apparent ante-partum infection but developed sepsis immediately following a planned cesarean section. There is nothing of particular interest about the third case.

Of the 2 remaining septic cases, one was proved at autopsy to have had a double uterus and was associated with toxemia, and the other was complicated by a placenta accreta. The latter patient delivered herself of a macerated fetus, but the placenta did not come away. There was no bleeding, the placenta remaining in situ until the day following delivery, when the patient's temperature rose to 103°F. An accreta was diagnosed after an unsuccessful attempt to remove the placenta; hysterectomy was performed, and general peritonitis developed.

It is gratifying that bungling operations played no part in these septic deaths. The handling of the case in which the Voorhees bag was employed unsuccessfully in a patient, six and a half months pregnant, who was finally delivered by vaginal cesarean section after sepsis had developed, is, of course, open to criticism. The case of ruptured uterus associated with sepsis was not appreciated until the autopsy was performed. There were no versions in the entire series.

Three points of particular interest evolve from this study: the small number of cases associated with injudicious operating; the increased number of autopsies over any previous year; and the disturbing fact that fatal sepsis occurred in 3 cases of planned repeat cesarean section, explainable only by inadequate aseptic technic—such deaths are regrettable and should never occur.

DEATHS

BLAKELY—DAVID N. BLAKELY, M.D., of Brookline, died October 15. He was in his seventy-sixth year.

Born in Campton, New Hampshire, Dr. Blakely attended Dartmouth College. After four years in Aintab, Turkey, he returned to this country and entered Dartmouth Medical School, receiving his degree in 1896. He spent four years at the Boston City Hospital and then practiced in Boston for several years. Dr. Blakely was assistant medical director of the New England Mutual Life Insurance Company at the time of his death. He was a fellow of the Massachusetts Medical Society and the American Medical Association. Dr. Blakely was active in the affairs of the Society for many years, having served as a member of the Council from 1918 to 1940 and as chairman of the Committee on Membership and Finance from 1922 to 1938.

His widow, a daughter, a son, a sister and a brother survive him.

GORMAN—JOHN W. GORMAN, M.D., of Brockton, died July 28. He was in his sixty-fifth year.

Dr. Gorman received his degree from the College of Physicians and Surgeons, Boston, in 1900. He was a former member of the Massachusetts Medical Society.

CORRESPONDENCE

THE APPROACHING REFERENDUM

To the Editor: On November 3 the voters of Massachusetts will have an opportunity of deciding at the polls whether physicians are to be allowed to practice their profession in accordance with the best medical standards or whether an old blue law on the statute books of the Commonwealth will continue to stand in the way of their saving the health and even the lives of some of their patients. The referendum to be voted on means just this: duly registered physicians shall be permitted to give contraceptive advice to *married* women whose *health or lives* will be jeopardized by pregnancy.

It is an established medical fact that pregnancy imposes a strain on a woman and that in the presence of many diseases (for example, heart disease, nephritis, tuberculosis, certain psychiatric conditions and so forth) continuation of pregnancy or repeated pregnancies may seriously damage the health or even kill some of these women.

It would seem superfluous, therefore, to argue the obvious desirability of this measure, especially before a medical audience, were it not for the devious, obscurantist and fallacious arguments that have been spread as a veritable school of red herrings across the path of truth and that may unfortunately confuse many people; these should be briefly answered.

It is believed by the Catholic Church that such contraceptive methods violate God's will and hence must not be used under any circumstances. This law will in no way interfere with those holding these beliefs; as the state Supreme Court itself has stated, the law is purely permissive, no Catholic physician or patient need use it. It merely extends to those not holding this religious belief a vital medical right, which a minority religious group would withhold from them.

It has been charged that the referendum promotes disunity and thus impairs the war effort. Actually the opposite is the case: true unity and true democracy only exist when the civil and religious liberties of all are protected and mutually respected. It is the opponents of this measure who are sowing disunity by perpetuating intolerance, and they are trying to maintain an economically undemocratic situation whereby the poor people of the State, who can only be adequately cared for in clinics, are deprived of medical help, which many of the well-to-do are now obtaining in one way or another.

The charge that this law will increase license and promiscuity is equally absurd, and is by implication a slur on the honor of the medical profession. Since it will apply only to married women for health reasons, any advice given to any other women will have no more legal sanction than exists at present. The hypocrisy of those making this charge is evident from the fact that they have never in concerted fashion publicly opposed the sale of condoms and similar articles which, it is well known, are the contraceptives chiefly used in sexual promiscuity; their sale has been declared legal because they can be sold ostensibly "for the prevention of disease." This measure will improve moral standards because it will give married women who need it the right to obtain, and physicians the right to prescribe, this advice *legally*.

Another accusation is that this law will lead to race suicide. It is patent that the number of healthy children that the women who will come under this law will fail

to produce is extremely small, and will be more than overbalanced by the increased number of viable children who will be born when sick mothers can properly space their children and limit the size of their families. Statistics prove our point: for example, in Ireland, where birth control has long been outlawed by church and state, the population has been cut in half during the last one hundred years, the most catastrophic birth decline of any nation in the world; on the other hand, in Holland, which pioneered in public birth-control clinics in 1880, the population has doubled in 60 years, owing to a much higher marriage rate and very low infant and maternal mortality rates. Other factors than the legality of contraceptive advice determine birth rates.

We often think with pride that Massachusetts ranks high in the medical world. But in this case all states in the Union except Massachusetts and Connecticut accord doctors the right to give needed advice. The challenge has been thrown down to the people of Massachusetts, and especially to physicians. It is an issue that far transcends the particular point with which this referendum deals. The issue is, Shall doctors be denied the right to practice their profession according to the highest medical standards and in accordance with the dictates of their own consciences?

WILLIAM H. ROBEY, M.D., *Chairman*

LAURENCE B. ELLIS, M.D., *Secretary*

Physicians Committee for the Defense of Medical Rights

143 Newbury Street
Boston

NOTICES

ANNOUNCEMENTS

DR. HENRY R. VIETS announces the removal of his office to 262 Beacon Street, Boston, on November 1.

The Bacteriological Laboratory of the Health Department of the City of Boston has been transferred from Room 1101, City Hall Annex, to new quarters in the Haymarket Square Relief Building, where the entire personnel of the Health Department will shortly be located. The Bacteriological Laboratory can be reached by the same telephone numbers, and maintains the same bacteriologic and serologic services, with the advantage of modern facilities and equipment.

MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Bigelow Amphitheater of the White Building on Tuesday, October 27, at 5 p.m.

PROGRAM

Some New Data on Oxygen Poisoning. Drs. C. M. Williams and H. K. Beecher.

Notes on the Action of Colchicine. Dr. Austin M. Brues.

The Relation of Vascular Disease to the Hypertensive State based on a Study of Renal Biopsies from 100 Hypertensive Patients. Drs. Benjamin Castleman and R. H. Smithwick.

17-Ketosteroids Excretion in Normal and Abnormal Children. Drs. N. B. Talbot and A. M. Butler.

(Notices continued on page viii)

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ECZEMA AND PRURITUS IN THE AGED*

LEONARD E. ANDERSON, M.D.†

SPRINGFIELD, MASSACHUSETTS

SINCE the average span of life has increased steadily and the population has come to be made up of a larger proportion of older people, medicine in general has paid more attention in the past decade or so to the problems presented by this group, and the term "geriatrics" has become commonplace in medical literature. Numerous problems peculiar to old age have been subjected to special study, and articles on a wide range of these have been published. Eczema and pruritus in the aged have not received a great deal of special attention in the literature largely because they present essentially the same problem in old people as in other age groups except for the clinical picture produced by senescent skin changes themselves.

The words, "eczema and pruritus," embrace a very wide field and in their discussion a whole treatise on general dermatology could properly be included, since a majority of dermatoses are eczematous or dermatitic and most are pruritic. This paper, however, is limited to the chief conditions producing a more or less generalized pruritus.

It might be well to make a few prefatory remarks about the mechanism of "itch." Itching is a distinctive cutaneous sensory disturbance peculiar to the integument and does not depend on the presence of cutaneous eruption for its existence. It is a complex sensation composed of a blending of touch and pain, and can be perceived only when both the touch and pain transmission tracts are functioning. It is apparently largely a thalamic rather than cortical sensory sensation and can occur in sleep and semiconscious states. Scratching during sleep in many of the pruritic dermatoses is, of course, a common observation. Perception of itch depends on an attention factor and a threshold susceptibility factor, the former con-

trols the slight sensations present in even normal skins, and these are therefore not perceived as itch. In long-standing pruritus, the threshold is lowered, and fatigue states affect the attention factor, so that the treatment problem is not an easy one.

It should first be said that a diagnosis of senile eczema or pruritus is too often made just because the patient is aged. Instead, as in younger patients, one should attempt to differentiate and classify the aged patient's condition. Even when one is presented with the picture of pruritus without gross cutaneous change in a thin, dry, aged and atrophic skin, the diagnosis of senile pruritus should not be made too readily without consideration and elimination of other possible explanations; the patient may have subthreshold jaundice, for example, from early obstruction by a cancer.

TYPES OF PRURITUS

Senile pruritus occurs in both men and women, usually over sixty years of age. This age is an arbitrary one, since, obviously, some patients have senescent cutaneous changes beginning at an earlier age and others have little discernible atrophy even in the sixties. The exciting cause of senile pruritus is atrophy of the entire thickness of the skin, including its appendages, which results in a thin, dry, irritable skin and leads to generalized itching.

Psychoses and psychoneuroses are primarily psychiatric rather than dermatologic problems, but the average practitioner can certainly do more even in an anxiety neurosis than dismiss the patient with the statement, "It's all in your imagination." Acarophobia (fear of scabies or imaginary infestation with mites or scabies) should be recognized because much can be accomplished by authoritative and convincing reassurance. A patient with acarophobia almost invariably picks

*Presented at a meeting of the Section of Dermatology and Syphilology, Massachusetts Medical Society, Boston, May 27, 1942.

†Assistant dermatologist, Springfield Hospital, dermatologist, Western Memorial Hospital.

from the skin pieces of lint, crusts and so forth, and is convinced that these are mites; he usually brings to the physician some of these specimens in a pillbox or carefully wrapped in paper. Even if the nature of the specimen is grossly obvious, it should be studiously examined with a lens or microscope, preferably in the presence of the patient. If the true situation is then explained and the patient reassured, this in itself effects a cure in most cases unless there is a deeper underlying "sense of guilt" or other psychiatric problem.

Diabetes can be diagnosed or ruled out by urinalysis and blood-sugar determination, and the glucose-tolerance test, if indicated. Diabetes does not produce a distinctive eruption in patients who have pruritus because of it. Carbuncles, furuncles and other pyogenic infections are likely to occur, but may be entirely absent in the patient presenting himself because of pruritus. Necrobiosis lipoidica diabetorum is a rare dermatosis observed in diabetic or prediabetic patients, but its appearance is so distinctive that it could hardly be mistaken for eczema and need not be discussed here.

Jaundice is a well-known cause of generalized itching, and no one would fail to recognize this relation in a fully developed icterus. However, it must be remembered that pruritus can be present and troublesome when the skin has no observable yellowish tint and the scleras appear normal. An icteric index determination is helpful, and a full medical workup from the standpoint of the biliary system should be done if indicated.

The *lymphoblastoma group* includes Hodgkin's disease, lymphatic and myelogenous leukemia, lymphosarcoma and mycosis fungoides. These are fortunately rare, but those who practice dermatology have at some time seen one or another of these in a patient who was considered to have "eczema." The clinical pictures are not distinctive enough to warrant taking time to attempt to describe or differentiate them, except in the tumor stage of mycosis fungoides. But even in the early stages of mycosis fungoides, which may last for years, a definite diagnosis cannot be made on clinical appearance alone. The type of patient who comes under the scope of this discussion usually presents a fairly extensive erythrodermia or exfoliative dermatitis. The skin may show definite infiltration, or this may not be evident; there may be an accompanying lymphadenopathy, and the pruritus may be intractable. Diagnosis depends on the study of the cellular constituents of the blood and on biopsy of the skin and lymph nodes. It must be borne in mind, of course, that the skin can show typical and pathognomonic leukemic infiltration in the presence of a normal picture in the circulating blood.

Dermatitis hiemalis (winter itch) and *bath dermatitis* can, for convenience, be considered together. They occur at any age, but the senescent dry atrophic skin is especially vulnerable. Although some persons apparently react with pruritus to cold itself, most patients have their dermatitis or pruritus because of excessive defatting and drying of their skins by means of soap and water and the dry overheated air of dwellings. The trunk and the extensor surface of the extremities are especially involved. Only the evidence of scratching and a mild ichthyotic change may be present, or a patchy dry superficial erythematous-squamous dermatitis, at times even eczematized. In warm weather, the condition is ameliorated or disappears because the overdried air factor is no longer operative, and perspiration partly assumes the role of lubrication carried on by sebaceous activity in younger skins.

Urticaria is distinguished by the presence of wheals, with which everyone is so familiar that the eruption cannot be confused with eczema. However, the persistence of urticaria is due to recurring crops of lesions, and the individual lesion may reach full development and undergo involution in a few hours, so that no trace of wheals may be present at the time of examination. A careful history, however, and subsequent observation establish the diagnosis and rule out senile pruritus. Giant hives or angioneurotic edema is a not infrequent accompaniment of chronic urticaria.

Drugs, such as morphine and cocaine, taken by addicts can produce generalized pruritus. History and concomitant findings point the way to the diagnosis. The various drugs used therapeutically that can produce a dermatitis medicamentosa or pruritus are too numerous to list in a paper of this scope.

Parasites that are most commonly encountered in this vicinity include scabies and pediculi. Scabies is produced by a macroscopically visible mite that burrows into the skin to deposit its ova. When a classic burrow is found, diagnosis is easy. Usually, however, scratching destroys these, and one must depend on the history and the distribution of the eruption. Itching is most intense after the patient is in bed, when the warmth of the bedclothes stimulates the mites to activity. The thin-skinned regions are characteristically involved, and the sites of predilection are as follows: finger webs, flexor surfaces of the wrists, axillary folds, waistline, buttocks, nipples (in women) and penis (in men). The face and neck are spared except in infants. The mite can be recovered from a burrow, but this is by no means as easy as most writers lead one to believe. There

are three common kinds of pediculi: *Pediculus capitis*, *P. corporis* and *P. pubis*. The first attacks only the scalp, and the diagnosis is made by the finding of the adult louse or "nits," which are sacs containing the ova and are attached to hair shafts. *P. pubis* attacks pubic hairs primarily, but is often found in the axillas, occasionally on the hairs of the chest and abdomen, and rarely in the eyebrows and lashes. The adult louse is easily seen with a lens at the base of a hair, with its head buried in the follicle. The nits are attached to hairs but are smaller than those of head lice. *P. corporis* does not live on the skin but in the patient's clothing, especially about the seams. It produces a nondescript scratch dermatitis especially about the shoulders, interscapular region, waistline and upper portions of the buttocks; diagnosis is confirmed by examination of the underclothes for the parasite. Chiggers, straw itch, tick bites and so forth are not prevalent in Massachusetts.

Psoriasis can be very pruritic when it is acutely generalizing. If small discrete lesions are present, the characteristic micaceous scale and capillary bleeding points can usually be found in well-developed lesions. When the process has turned into a universal exfoliative dermatitis, as it does only rarely, diagnosis cannot be made without the help of biopsy or previous knowledge of the pre-existing psoriatic eruption.

Lichen planus is characterized by pruritus, but diagnosis is easy even in extensive eruptions because of the presence of violaceous polygonal flat lichenoid papules with a characteristic sheen and almost no scale. When the papules are large or confluent, fine grayish lacelike streaks (known as Wickham's striae) are usually easily seen and are practically pathognomonic. In the extremely rare case in which lichen planus evolves into a universal exfoliative dermatitis, the diagnostic problem is the same as in psoriasis.

Dermatitis herpetiformis is a rare dermatosis of multiform character but showing almost always some herpetiform, grouped vesicles. It runs a chronic course, and the skin tends to become pigmented at the sites of involvement. It is often extensive but not universal, and sites of predilection are the extensor surfaces of the extremities, the midline of the back, the shoulders, and the back and sides of the neck. Diagnosis is suggested by chronicity, pigmentation and herpes-like grouped vesicles or blebs.

Contact sensitivity to wool or other articles of clothing can produce pruritus or eczematous eruptions. Careful history taking and indicated patch-test studies are essential for a positive diagnosis.

TREATMENT

In general, treatment should be aimed at the causative and contributing constitutional and psychoneurogenous factors in generalized itching, and antipruritics used as adjuncts.

Of the antipruritics, phenol, menthol, camphor and liquor carbonis detergens are in widest use and least likely to do harm. The cocaine derivatives include benzocaine, nupercaine, butyn, diathane hydrochloride and bolocaine, all of which not uncommonly produce contact dermatitis after the patient's skin has developed a sensitivity to them, and should be avoided if possible. Witch-hazel water and alcohol have antipruritic value, and plain hot or ice water often controls a localized itching bout. The cornstarch or oatmeal bath is useful in generalized itching and should usually be followed by the application of an oily lotion.

In senile pruritus and other pruritus without dermatitis, local medication in the form of a lotion may be employed. Although many more elegant formulas can be made up, the unavailability of their newer ingredients in neighborhood pharmacies is a distinct disadvantage so that the time-honored Pusey's calamine liniment is still a useful preparation:

R	Liquid phenol	1.0 cc.
	Oil of bergamot	1.3
	Powdered tragacanth	5.3 gm.
	Zinc oxide	
	Calamine	aa 30.0
	Olive oil, 150.0 cc., or	
	liquid petrolatum	90.0 cc.
	Water	q. s. ad 480.0

Make an emulsion of the oil with tragacanth. Add gradually, with constant shaking, the other ingredients already mixed.

For patients with winter or bath itch, the cornstarch bath is substituted for soap bathing, and the following lotion is prescribed:

R	Starch	8.0 gm.
	Glycerin	4.0
	Witch-hazel water	16.0 cc.
	Oil of sweet almond	60.0
	Olive oil	
	Lime water	aa q. s. ad 240.0

If the antipruritic effect needs to be enhanced, 1 to 2 per cent phenol and 0.5 or 0.25 per cent menthol or camphor may be added; or the following lotion, which contains tar, may be substituted:

R	Phenol	2.4 cc.
	Camphor	1.2 gm.
	Glycerin	2.4 cc.
	Liquor carbonis detergens	7.2
	Starch	12.0 gm.
	Olive oil	
	Lime water	aa q. s. ad 240.0 cc.

For the dry erythematous squamous dermatitic patches in these patients, the following ointment may be prescribed:

℞ Salicylic acid	0.3 gm.
Liquor carbonis detergens	3.0 cc.
Aquaphor	
Rose water ointment āā q. s. ad	30.0 gm.

If lichenification is present in chronically scratched areas, 5 to 10 per cent oil of cade or pine tar may be used in the above formula; or crude coal tar ointment may be prescribed as follows:

℞ Crude coal tar	2.0 cc.
Zinc oxide	2.0 gm.
Mix and let stand 24 hours	
Starch	8.0
Yellow petrolatum q. s. ad	30.0
Make an ointment	

If the patches are frankly eczematized, the following formula is useful:

℞ Ichthyol	0.9 gm.
Zinc oxide ointment	30.0

For scabies, an ointment containing sulfur and balsam of Peru is efficacious:

℞ Precipitated sulfur	12.0 gm.
Balsam of Peru	12.0 cc.
Lanolin	30.0 gm.
Benzoinated lard q. s. ad	120.0

For children, betanaphthol may be substituted for the sulfur in a strength of 3 to 5 per cent, an equal concentration of Peru balsam being employed. Successful cure depends on careful instruction of the patient. A hot soap bath should be taken the first night, and all crusts and vesicle tops scrubbed off; the ointment should then be rubbed into the entire skin surface from the neck down. On the next morning and night, the ointment is reapplied, and on the following morning, a hot soap bath is taken and all underclothing and bed linens cared for by boiling or dry cleaning. One of the above oily lotions may be used if there is irritation from the treatment course. One course rarely fails to cure and, in any event, should not be repeated in less than ten days.

P. capitis is best treated by the time-honored turbaning of the scalp with equal parts of olive oil and kerosene overnight, followed by shampoo and removal of the nits by soaking with vinegar and the use of a fine-tooth comb. *P. corporis* requires attention to the clothing and one of the above lotions for the scratch dermatitis. *P. pubis* should not be treated with blue ointment because of the intense irritation provoked, but mercury may be used as a 1:500 solution of the bichloride and the nits soaked off with vinegar.

Generalizing psoriasis must be treated with caution, and no vigorous antipsoriatic medications should be employed. Autohemotherapy is useful at intervals of three to seven days; the starch bath may be used and followed in the guttate variety by an ointment containing 2 per cent each of salicylic acid and ammoniated mercury in a cold cream or Aquaphor base.

In lichen planus, irradiation is of distinct help but should be employed by an expert only. Mercury or arsenic by mouth or injection is indicated. A combination of the two metals in the form of mercury salicylarsenate (Enesol) is widely used intramuscularly, but occasional reactions occur. Local applications are of little avail and are indicated only to control pruritus.

Dermatitis herpetiformis is notoriously resistant to treatment, although some promising results have been obtained with the sulfonamides. Sulfur baths (a 2.5-cm. cube of commercial sulfurated potash being added to the tub), antipruritic lotions and arsenious acid by mouth in the form of Asiatic pills often produce a remission.

SUMMARY

Eczema and pruritus in the aged present the same problems as in other age groups, in addition to the factor of dry atrophic skin with increased vulnerability.

Generalized pruritus is produced by numerous conditions, and the diagnosis of "senile pruritus" should be made only after other causes have been searched for and excluded.

Therapy should not only consist of local applications but also aim at the underlying factors.

20 Maple Street

INTRACRANIAL ANEURYSM OF THE INTERNAL CAROTID ARTERY*

T W BOTSFORD, MD†

BOSTON

RECENTLY, a patient suffering from an intracranial aneurysm of the internal carotid artery entered the Peter Bent Brigham Hospital. So much interest was aroused from the study of this patient that I was stimulated to search out and review all similar cases admitted to the hospital, as well as those reported by others, in an effort to arrive at the proper management of this unusual condition. This paper is presented to summarize the findings and to report in detail on the most recent case.

CASE REPORT

A 51-year-old married woman entered the Surgical Service on June 9, 1941, complaining of a buzzing noise over the left side of her head of 4 months' duration. The past history was essentially irrelevant. The patient had always enjoyed good health. There was no history of syphilis.

Four months before entry, the patient awoke in the morning with a severe headache. She had had numerous headaches for many years and did not consider it unusual. That night, when she bent over to untie her shoelaces she suddenly had the sensation of a light bulb bursting in her head. This sensation lasted only a few seconds, but immediately afterward, for the first time she was conscious of a rhythmic buzzing noise over the entire left side of her head. This noise was present constantly thereafter and often kept her awake at night. Four weeks before admission, she noticed that she had double vision, and 3 weeks later, she had a single momentary sensation like an electric shock, in her right arm. There were no convulsions, hemiparesis or bouts of unconsciousness at any time.

Physical examination on admission showed an intelligent, well-developed and well-nourished woman in no distress. There was a loud bruit, systolic in time over the left side of the head anteriorly and over the left common carotid artery. A systolic thrill was palpable over the left common carotid artery. The lateral rectus muscle of the left eye was paralyzed, but the other extraocular muscles were normal. The pupils were equal and reacted normally to light and accommodation. Ophthalmoscopic examination showed normal eye grounds, and the visual fields were normal. The blood pressure was 130/90. Abdominal and pelvic examinations were negative. Complete neurologic examination was negative except for paralysis of the 6th cranial nerve on the left.

Examination of the blood showed a red cell count of 4,800,000 with a hemoglobin of 80 per cent (Sahli), and a white cell count of 6700. The blood volume was normal. Lumbar puncture showed normal pressure and normal dynamics. The cerebrospinal fluid was water clear and showed no increase in white cells and no red blood cells. The spinal fluid protein was 35 mg per 100 cc. Wassermann and Hinton tests on the blood and spinal fluid were

negative. X-ray films of the skull, chest and heart showed no abnormalities.

The impression on admission was that the patient had an intracranial aneurysm of the left internal carotid artery.

While the patient was in the hospital, the left common carotid artery was compressed for 20-minute periods on two occasions, without noticeable mental or physical changes. It was then believed that she could stand ligation of the left internal carotid artery.

Under local anesthesia, the left internal carotid artery was exposed. Diodrast was injected, and films of the skull were then made. Following this, the artery was divided, and the ends were ligated with silk. The murmur and thrill immediately disappeared, both subjectively and objectively. The report of the x-ray films of the skull was as follows:

Films of the skull in the operating room after injection of 70 per cent Diodrast show the left internal carotid artery well outlined, appearing normal up to the area beside the sella, where there appears to be vascular dilatation 1.5 cm in diameter. The upper edge of this, however, is not raised above the sella as is usual in aneurysms. The internal carotid artery beyond this point is not visualized.

After operation, the patient made an uneventful recovery. A minimum diplopia continued, as did the left 6th nerve palsy, but the bruit remained absent. At follow-up 7 months later, the bruit was still absent, and there had been a constant decrease in the patient's diplopia until it occurred only when she turned sharply to the left. The patient had learned to avoid this maneuver and therefore was not troubled by diplopia. The vision in the left eye was equal to that of the right, but there still remained weakness in the external rectus muscle on that side, presumably evidence of continued slight impairment of the 6th nerve function.

PREVIOUS CASES

This review of cases includes only the aneurysms located at the junction of the internal carotid artery, either at the circle of Willis or in close proximity to that region. Forty such patients, including the one reported above, have entered this hospital in the last twenty-eight years. Twenty-one cases were verified at operation or autopsy, and 19 were diagnosed clinically. One case, in addition, was verified by Diodrast injection of the internal carotid artery. Over three-fourths of the cases occurred in females; there were 31 females and 9 males in the group. The cases showed a marked peak in the sixth decade of life (Fig 1). There were twenty-seven aneurysms on the right side and thirteen on the left.

The symptoms of 36 patients, exclusive of the 4 whose aneurysms were found incidentally at autopsy, were abrupt in onset in 19 cases and in-

*From the Surgical Clinic, Peter Bent Brigham Hospital.

†Instructor in surgery, Harvard Medical School; fellow in neurology, Peter Bent Brigham Hospital.

sidious in 17. Headache and eye complaints were always the leading symptoms.

The third cranial nerve was involved in 23 cases (64 per cent): alone in 5 cases; with the fourth and sixth nerves in 9 cases; with the fifth nerve in 4 cases; with the fourth nerve in 2 cases; with the sixth nerve in 1 case; and with the fourth, fifth

this patient died six months later, and autopsy showed thrombosis of the aneurysm. Of the other 2, one patient was alive and asymptomatic at the end of five years, but has not been traceable since; the other is alive seven months after operation and free of the bruit, although she still has a residual sixth-nerve palsy.

In the untreated group, 9 patients (23 per cent) died of rupture of the aneurysm, 14 died without the exact cause being known, and 14 are unaccounted for, since they did not respond to follow-up inquiries.

DISCUSSION

Intracranial aneurysms have been the subject of considerable interest in the literature of the past few years. Some of the cases in this series have been reported by Symonds,⁴ Doubler and Marlow,⁵ Viets⁶ and Sosman and Vogt,⁷ because of interest in clinical manifestations and x-ray findings. Not until recently has an accurate clinical diagnosis of intracranial aneurysm been made. The gradual accumulation of knowledge concerning the disease and roentgenologic studies^{7, 8} of the appearance of intracranial aneurysms, including cerebral arteriography introduced by Moniz,⁹ have made this possible.

The syndrome of headache, either acute or recurrent, associated with paralysis of the third, fourth, fifth and sixth nerves, either individually or in combination, is strongly presumptive evidence of intracranial aneurysm of the internal carotid artery. The bruit must be searched for and, if present, is pathognomonic of the condition. Plain x-ray films of the skull may show calcification in the wall of the aneurysm. These areas of calcification are usually fine curvilinear shadows. In addition, there may be erosion of the bone adjacent to the aneurysmal sac.⁷ So far as I know, there is no danger in injecting Diodrast into the internal carotid artery to visualize the aneurysm, and the vessel can be ligated at the same time.

Rupture of the aneurysm, in some cases, may be the first manifestation of the difficulty: there is sudden, severe pain along the distribution of the trigeminal nerve as the blood is spilled over the gasserian ganglion, and coma usually follows. On examination, the neck is stiff, and Kernig's sign is positive. If lumbar puncture is done, the spinal fluid is found to contain fresh red blood cells. Death usually follows rupture, although Fearnside¹ reported that 41 per cent of his patients had one or more bouts of leakage from the aneurysm, without death.

The treatment of intracranial aneurysms has been directed toward the induction of thrombosis of the aneurysm. This has been attempted by

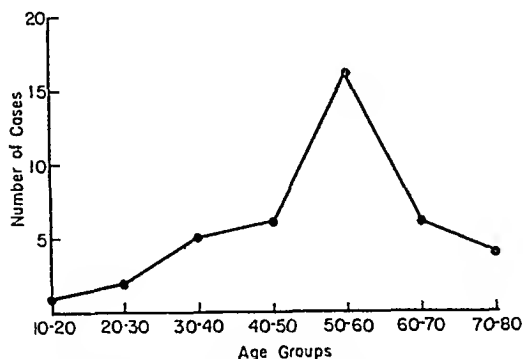


FIGURE 1. Incidence of Aneurysms at the Junction of the Internal Carotid Artery, according to Age Groups.

and sixth nerves in 2 cases. The sixth nerve only was paralyzed in 2 cases, the fourth and fifth in 1, and the fourth, fifth and sixth in 1.

Although these 27 patients presented ophthalmoplegia of varying degrees, of the 9 cases remaining, 3 were totally blind, 3 had homonymous hemianopsia, and 3 entered in coma. Nineteen patients had hypertension, and 17 had normal blood pressure. The blood Wassermann reaction was negative in all. The absence of syphilis in patients with intracranial aneurysm, in contrast to patients with aneurysms elsewhere, has been pointed out by others.¹⁻³

The presence of a bruit in the head was carefully searched for, both subjectively and objectively. Only 3 patients noticed a "buzzing noise" in the head, and in only 1 was it the chief complaint. In addition to these, a bruit over the skull was discovered by auscultation in 3 cases, so that in 6 (15 per cent) of the cases this sign was present.

The diagnosis on admission in 28 cases was intracranial aneurysm; in 5 cases, pituitary adenoma; and in 3 cases, meningioma. The neighboring symptoms, sometimes caused by a large intracranial aneurysm, may easily simulate a brain tumor, as pointed out by Symonds.⁴ In 1 case, not included in this series, a diagnosis of intracranial aneurysm was made, but at operation elsewhere the source of the trouble was found to be a chromophobic adenoma of the pituitary gland.

Only 3 patients were subjected to surgical therapy. In each case, the internal carotid artery was ligated in the neck. In 1 case, the aneurysm was also opened, and muscle was packed into the sac;

direct attack on the aneurysm, by ligation of the cervical portion of the internal carotid artery and by ligation by clip of the vessel distal to the aneurysm intracranially, in addition to ligation of the internal carotid artery in the neck. The direct attack on the aneurysm is usually impossible and is most dangerous.

Ligation of the cervical portion of the internal carotid artery for aneurysm was first practiced by Sir Astley Cooper in 1805. It is not a hazardous procedure in selected cases, and following it, a number of patients with intracranial aneurysm have had symptomatic relief. Schorstein,¹⁰ who collected 60 cases of intracranial aneurysms for which the internal carotid artery had been ligated, found that in infraclinoid aneurysms ligation was a benign procedure unattended by neurologic complications or death. However, in supraclinoid aneurysms, there was a 13 per cent mortality. This mortality he ascribed to the fact that there had been recent leakage from the aneurysm or compression of the basal arteries.

Before the internal carotid artery is ligated, it should be totally occluded by pressure for ten minutes, as recommended by Matas¹¹ and by Dandy,¹² to determine whether or not there is any untoward effect on the cerebral circulation. Occasionally, even after the occlusion test, a late effect may follow ligation of the artery. The preoperative condition of the cerebral circulation is all important in the decision of whether the patient will tolerate ligation of one internal carotid artery.

Dandy, in 1937, first trapped an intracranial aneurysm between a silver clip distal to it and a ligature around the cervical portion of the internal carotid artery. Since then, a few similar successful cases have been reported.¹²⁻¹⁴ It is a difficult procedure at best and not always possible; nevertheless, it is the rational method of approaching the disease.

SUMMARY AND CONCLUSIONS

A case of intracranial aneurysm of the internal carotid artery, associated with a bruit over the

head and a sixth-nerve palsy, is reported. Treatment consisted in ligation of the cervical portion of the internal carotid artery.

The cases of 40 patients with aneurysm of the intracranial portion of the internal carotid artery who entered the Peter Bent Brigham Hospital in the last twenty-eight years were reviewed.

Headache and palsy of the third, fourth, fifth and sixth nerves were the leading clinical signs and symptoms. A bruit over the head was present in 15 per cent of the cases.

Ligation of the cervical portion of the internal carotid artery is advocated, provided that the cerebral circulation is sufficient after occlusion of the artery for ten minutes.

Trapping the aneurysm between an intracranial clip and a ligature around the cervical portion of the intracranial aneurysm may be attempted, but is not always possible to carry out.

Cerebral arteriography is a safe and reliable procedure to verify the presence of the aneurysm.

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GASTROINTESTINAL SYMPTOMS AND INGUINAL HERNIA*

ROBERT S. MYERS, M.D.,† AND ROBERT ZOLLINGER, M.D.‡

BOSTON

BEFORE operation is advised for an inguinal hernia, it is an established practice to make certain that the patient does not also present evidence of chronic pulmonary disease or partial urinary obstruction. Little significance, however, has been attached to gastrointestinal symptoms. Such symptoms occurring in patients with inguinal hernia should receive careful study. There is a tendency to attribute these complaints to the presence of the hernia and to advise repair without further investigation. This, we believe, is a dangerous policy, for not infrequently some other process, such as ulcer or cancer of the gastrointestinal tract or gall-bladder disease, is masked by the more obvious complaint of hernia.

Much of the literature suggests that gastrointestinal symptoms, such as epigastric distress, abdominal cramps, flatulence, nausea and vomiting, may be the result of an inguinal hernia that has never been incarcerated or strangulated. An uncomplicated inguinal hernia is said to produce distress varying from uneasiness in the epigastrium to actual abdominal pain in the region of the umbilicus. Nausea has been alleged to result from traction on the mesentery, and reflex disturbances of digestion—cramps, intestinal pain and gas—are described.¹⁻⁴

On the other hand, there are those, like Behan,⁵ who believe that pain, usually of a dragging nature, is of minor importance as a symptom of uncomplicated inguinal hernia. Andrews and Bissell⁶ state that in at least 90 per cent of all cases of hernia pain is totally absent. In their opinion, the relief of chronic indigestion supposed to be caused by hernia has proved to be very disappointing, for it generally persists after the hernia has been surgically cured.

There are thus two opposing schools of thought: one believing that gastrointestinal symptoms can be the result of simple uncomplicated inguinal hernia; and the other that gastrointestinal symptoms are not to be explained by such an obvious reason.

Within recent months, our attention has been arrested by 2 cases of gastrointestinal cancer, overlooked at the time of herniorrhaphy. This led us to review 200 consecutive cases of uncomplicated

inguinal hernia coming to operation. In studying these cases, we found that in 81, or 40 per cent, there were no complaints other than the presence of a hernia; 82 patients, or 41 per cent, had groin pain, and 37, or 18 per cent, had definite gastrointestinal symptoms that required investigation (Table 1). Thus, approximately one fifth of the

TABLE 1. *Gastrointestinal Symptoms in Cases of Operable Inguinal Hernia.*

GASTROINTESTINAL SYMPTOMS	NO. OF CASES	PERCENTAGE OF TOTAL
Not present	81	40
Present but mild (groin pain only)....	82	41
Present	37	18
Apparent cause	22	11
No apparent cause	15	7
No cancer postoperatively.....	13	6
Cancer postoperatively.....	2	1
Total	200	

patients had symptoms referable to the gastrointestinal tract, and it is with this group that we are primarily concerned.

Table 1 shows that 22, or 59 per cent, of the 37 patients with gastrointestinal symptoms had a plausible explanation for their complaints of abdominal pain, gas, nausea or vomiting. These were the following: momentary attacks of recognized incarceration, whose reduction relieved all symptoms; epigastric distress treated successfully by diet and alkalis that were prescribed by the family physician; and gall-bladder disease and peptic ulcer, proved by x-ray examination.

Fifteen, or 41 per cent, of these patients presented vague but persistent gastrointestinal symptoms for which no cause was found prior to operation. There was no history of incarceration; diet and medical treatment brought no relief; and x-ray examination was negative in the few cases in which it was employed. Although it is true that 11 patients in this group were relieved of symptoms following herniorrhaphy, 2 of the 15 demonstrated gastrointestinal cancer as the true basis for their complaints. If the error of first performing herniorrhaphy on a patient who also suffers from carcinoma is to be avoided, all unexplained gastrointestinal symptoms must have a thorough appraisal before operation. A review of the following cases clearly shows the need for intensive investigation of gastrointestinal symptoms in the presence of inguinal hernia.

*From the Surgical Clinic, Peter Bent Brigham Hospital.

†Instructor in surgery, Harvard Medical School; associate junior surgeon, Peter Bent Brigham Hospital.

‡Major, M.C., A.U.S.; formerly, surgeon, Peter Bent Brigham Hospital.

CASE 1 A 48 year-old man was admitted to the hospital complaining of a right inguinal hernia of 6 weeks duration. He had experienced occasional dragging pain in the right groin, gas and sour eructations. Physical examination was not remarkable except for a right indirect inguinal hernia. Herniorrhaphy was performed, and convalescence was normal. After discharge from the hospital gaseous eructations and epigastric distress continued. The patient was studied in the Out Door Department and the stools were found to be strongly positive for occult blood. X-ray studies suggested carcinoma of the stomach. The patient was therefore readmitted, 5 months after herniorrhaphy for gastric resection for carcinoma. During the 2 month interval since gastric resection, he has had no gastrointestinal symptoms.

CASE 2 A 58 year old man was admitted to the hospital complaining of bilateral inguinal hernias of 3 years duration. These had been increasing in size prior to admission and were especially prominent when the patient strained at stool. The patient complained of chronic constipation, and had recently been taking increasing daily doses of laxatives. There were no groin symptoms, abdominal pain or weight loss. Physical examination showed bilateral inguinal hernias, for which bilateral herniorrhaphy was done. At the time of operation, a hard nodule was noted in the right hernial sac, which was removed for microscopic study. A metastatic carcinoma was reported which was thought to have arisen from the gastrointestinal tract. Following recovery from herniorrhaphy, a barium enema demonstrated an obstructive lesion of the sigmoid. Subsequently, at an abdominal exploration carcinoma of the sigmoid, with diffuse peritoneal metastases was discovered.

These 2 cases are but examples of the pitfalls hidden by apparently simple cases of inguinal hernia. Behind the mildest symptoms may lurk serious disorders detrimental to the patient's health. This is especially true in the middle aged and the elderly, since advancing years bring on an increased incidence of serious constitutional disease. Both urinary obstruction and chronic cough are well recognized contraindications to herniorrhaphy, and efforts are made to remedy or control these conditions previous to operation. The physician and patient, however, are only too willing to assume that the presenting inguinal hernia is the sole cause for the patient's indigestion and to proceed with herniorrhaphy without further investigation. We believe that ulcer in the younger age groups and gall bladder disease and cancer in the middle aged or the elderly must be carefully ex-

cluded in patients with inguinal hernia with gastrointestinal symptoms before the hernia is repaired.

Obviously, it is impractical and financially impossible to subject every patient with an inguinal hernia and gastrointestinal symptoms to complete roentgenologic examination, however desirable this may be. But there are simple methods that will narrow down the field until only a few remain who demand further investigation. A painstaking history with special reference to the nature of the gastrointestinal symptoms and their duration often indicates patients in whom ulcer, gall bladder disease or cancer is to be suspected. A thorough general physical examination is, of course, essential. Abdominal masses and tenderness should be sought. Rectal examination must be most thorough, and should include not only a careful evaluation of the size, shape and consistence of the prostate but also a search for masses suggestive of carcinoma in or about the rectum. Laboratory studies, including those of the blood, stool and urine, are indispensable. The finding of occult blood in a stool specimen, as illustrated in Case 1, may be the clue that abnormalities other than the hernia are present. If such measures fail completely to explain persistent gastrointestinal complaints, then the physician must carry out further investigation by x-ray.

CONCLUSIONS

Gastrointestinal symptoms occur in approximately one fifth of the patients with inguinal hernia. These symptoms, if well established, may indicate basic or antecedent causes other than hernia. The cause for such symptoms must be completely explained before operation for inguinal hernia is advised.

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EMERGENCY MEDICAL SERVICE FOR A SMALL CITY

FREDERICK T. HILL, M.D.*

WATERVILLE, MAINE

IN the setting up of an emergency medical service for civilian defense, it seems decidedly advantageous to take into consideration the medical facilities and personnel that might be available. Frequently, the small community is confused, and perhaps overwhelmed, by stereotyped plans laid down by state and national authorities

more first-aid squads, and to establish first-aid posts near the scene of any incident. Stations are also prepared to handle minor cases not requiring hospitalization.

Each hospital was asked to appoint an executive medical officer, to be in charge of medical personnel, and an admitting officer, to be in charge of

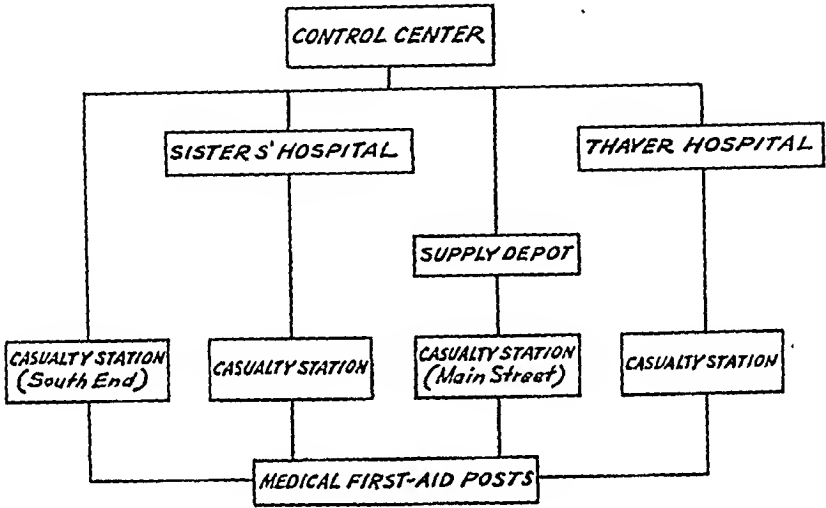


FIGURE 1.

—plans that might be possible of execution in a large city but are quite impractical for the smaller place. When one remembers the constantly diminishing supply of physicians, as more of the younger doctors are called into service, it becomes increasingly imperative that any emergency medical service be adapted to local conditions.

It was my lot to be drafted to reorganize such an emergency medical service in Waterville, Maine, a small city. The previous attempts to pattern the service on stereotyped plans had not been productive of satisfactory results.

The first step in the new plan was the utilization of the two hospitals in the city not only as casualty receiving hospitals but also as casualty stations and to furnish pools of physicians and nurses. In addition, two other casualty stations were set up to take care of sections not readily covered by the hospitals. A supply depot was established at the most centrally located casualty station.

Each casualty station, including the hospitals, is to be prepared to send out medical squads consisting of 1 physician, 1 or more nurses and 1 or

patients admitted because of an emergency. Provision was made for alternates. It was stated that these should be physicians of experience and executive ability, able to size up situations and make decisions quickly.

The executive medical officer specifies the duties of the physicians at his station, such as dressing room, shock room, fractures, burns and major surgery; naturally, these assignments will vary according to the type of admissions and the personnel available. He assigns physicians to be in charge of first-aid posts, when requests for such posts are received from the control center. He should exercise due judgment regarding the size and make-up of each squad, depending both on the information received of the extent of the incident and on his available supply of physicians. The executive medical officer should make a list of all physicians, nurses, first-aiders and so forth reporting at his station. This should be available for the medical service when the mobilization is over.

The admitting officer should be a physician of keen clinical judgment. He will examine cases on admission and assign them to the proper department.

*Chief of staff, Thayer Hospital; chief, Emergency Medical Service, Office of Civilian Defense.

Each hospital will be notified by the control center on the yellow signal and should then proceed to ask certain of its medical personnel to assemble before the red signal. On the blue signal, the control center will ask each hospital the number of available beds. On this signal, all physicians, nurses, first aiders and ambulances are requested to report to their stations. On the red signal, stations will telephone the control center, reporting the number of physicians, nurses and first aiders at their posts.

The chief medical officer, with an assistant to act as clerk, handles the service from the control center. Two other physicians are familiar with this phase of the work and will be able to take charge in his absence. In fact, all key positions in the service are covered "three deep."

Three physicians are assigned to each of the casualty stations. The staffs of the two hospitals cover their respective institutions, furnishing personnel for the casualty stations, first aid posts and the hospital itself. Graduate nurses and first aid squads are assigned to each of the four stations. Three ambulances are assigned to each hospital, and two to each of the other stations. One or more dentists are assigned to each of the hospitals and stations.

Since, in the event of an emergency, a great deal of difficulty and confusion may be caused by distracted and hysterical relatives and friends, members of the clergy—one Catholic priest and one Protestant clergyman—have been assigned to each of the stations. An emergency morgue, in charge of an official of the Police Department, and with a Catholic priest and Protestant clergyman assigned to it, has been set up in the Municipal Armory. The supply depot, in which the reserve medical and surgical supplies, reserve emergency chests and so forth are kept, is in charge of three lay persons who are experienced in this work and who are responsible for the medical equipment of the ambulances. A pool of extra ambulances is assigned to this supply depot. The supply depot has also been charged with the responsibility of maintaining an adequate supply of various drugs, such as tetanus antitoxin and so forth, at the casualty stations. Plasma in adequate amounts is kept in storage at the two hospitals.

Telephone service must be maintained at an efficient level. When an incident requiring medical service is reported to the control center, the chief medical officer will notify the most available casualty station. The telephone operator takes the message in writing, repeats the message to the center for check, and immediately transmits it to

the executive medical officer, who then dispatches one or more medical squads to the scene. As soon as this is done, the telephone operator notifies the control center as follows: "One (two) squad(s) to ——— St. at — p m."

On arrival of the squad at the incident, a first-aid post will be set up in the most convenient location, the main essentials being light, water and communications (telephone). The squad will call its own station (hospital) if additional personnel, supplies and so forth are required and, if possible, will notify the hospital if cases are to be sent in. The executive medical officer at the station will notify the control center if an additional squad is dispatched.

If any station (hospital) is unable to furnish needed personnel or supplies, or is being depleted by the sending out of squads, the executive officer should notify the chief medical officer at the control center, who will send personnel, supplies and so forth from other stations or the supply depot.

Tags will be filled out as much as is practical at the first-aid posts. Naturally, there should not be undue delay in sending very seriously injured persons to the hospital, and many data can be obtained later at the hospital. All emergency treatment given, such as the injection of morphine or the application of a tourniquet, should be noted by marking "U." Hospitals should keep records of all cases admitted in the casualty record books furnished for this purpose.

All personnel should remain at the stations until "cleared" by the chief medical officer at the control center.

Three mobilizations, with simulated incidents, are conducted each month, in addition to a series of meetings for the entire medical service at which pertinent problems, such as "first aid posts," "casualty stations," and "treatment of gas casualties," are discussed. It has become obvious that the main problem is one of co-ordination between the physician, the nurse and the first aid squad. The average physician knows little about setting up or handling a first aid post. He can take care of one casualty, but is quite at a loss when confronted with ten or twelve. Yet he is in charge and should be familiar with these problems. It is only by practice, constructively criticized, that this matter can be worked out efficiently. A system of observers—physicians competent in handling these situations—has been employed. These men not only criticize but also give instruction to the doctor, the nurse and the first aid squad.

The first aid organization is under the direction of a corps director and consists of five squads one

assigned to each station and one held in reserve. Each squad is commanded by a squad leader, who is a qualified instructor. Each squad consists of four units of four men under a unit leader, who holds a Red Cross advanced certificate. One unit of each squad functions at the station, making tag records, assisting nurses, preparing dressings and splints and taking charge of patients' clothes and personal effects. Two units are allocated to ambulance duty, and one unit is held in reserve. Definite duties are assigned to each unit member, such as responsibility for ambulance equipment and splints, and the members are trained to act as a unit in handling casualties. These squads are all under the command of the corps director, who is responsible for this training. We have been for-

tunate in having as a director a man who has had a long experience as an instructor in first aid at the mill of a paper company that has long been recognized for its efficiency in first-aid and safety work. The director has been able to bring with him as squad leaders men who have served under him as instructors. One such squad of trained first-aiders, working under a capable leader, is worth more than a large number of well-meaning but inexperienced amateurs.

So far this plan seems to be working out very well. It is not suggested as anything new or ideal, but as a means by which a small city with limited medical personnel can meet the emergency.

Professional Building

IS TUBERCULOSIS INCREASING?*

JOHN A. FOLEY, M.D.†

BOSTON

FOR several years, the opinion has been prevalent that tuberculosis is decreasing and that the fight against this disease has finally made definite headway. To those who are working in the field, however, there seems to be another view. At the Boston Sanatorium, the largest hospital devoted to the care of the tuberculous patient in Massachusetts, we have had an experience, over the past five years, that leads us to think that other factors have not been considered.

The total number of patients treated in 1936 was 1079; in 1937, 1088; in 1938, 1082; in 1939, 1042; in 1940, 1070; and in 1941, 1110. These patients came from two sources, the Boston Health Department and the Boston City Hospital. According to these figures, there has been a gradual increase in the admissions to the Sanatorium since 1939. The number of minimal cases consistently remained approximately 10 per cent up to 1939, when it decreased to 8 per cent; in 1940, it was 8 per cent and in 1941 7 per cent. Hence, as the total number of treated cases increased, the number of minimal cases decreased and the number of moderately advanced cases increased. This indicates either that the cases are not being discovered early enough or that the patients are not being sent for treatment until they are well along

in the disease. It is pertinent to say that the minimal cases are usually discovered by extensive studies on large groups or by the study of contacts of known cases, whereas the great majority of the moderately advanced cases are picked up as the result of hospitalization for other conditions, or as the result of neglect on the part of the patient to consult his physician in time. This is equally true of the far-advanced cases.

In 1941, 29 per cent of the patients with tuberculosis who died in Boston were not reported to the Health Department until after death, and 13 per cent were reported within a month before death; the disease should have been discovered early enough to ensure information to the Health Department. In short, in 13 per cent of the known deaths from tuberculosis, the patients had no health supervision, no checkup of contacts and no restriction of activity until a month before death, and 29 per cent had no supervision whatsoever. From what is known about this disease, these patients were potentially disseminators of the tubercle bacilli for a number of months before death. When this situation is appreciated, it is not difficult to understand why 55 to 60 per cent of the deaths in 1941 at the Boston Sanatorium occurred before the patients had been at the hospital six months; their cases were so far advanced that no treatment could avail. This was not unique for 1941; it has been the same story during the last five years.

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†Clinical professor of medicine, Boston University School of Medicine; director of Fifth and Sixth Medical Services, Boston City Hospital; chief of staff, Boston Sanatorium

This is not an isolated example of the belated discovery of tuberculosis. The May 16, 1942, issue of the *Journal of the American Medical Association* reports that of 594 men rejected for tuberculosis by the selective-service boards of Illinois, only 21 had previous records reported to the State Board of Health. At the Boston Sanatorium, 15 patients have been referred after having been rejected by their local selective-service or induction boards, few of whom suspected that they were infected. All this leads one to believe that tuberculosis will never decrease until the carriers are discovered and regulated. This will be accomplished for the male population, in a large measure, by the examinations preceding induction. This still leaves the female population to be studied; a number of these will fall into the contacts of diseased males and will be picked up in this way.

The main effort must be made with younger age groups, in the junior high schools and the secondary schools. This group should be tuberculin tested, and the reactors examined by x-ray and reported to the health authorities for follow-up. It is a simple matter for the family physician to apply a patch test, read it, and have a reactor x-rayed, but most men are reluctant to report the minimal case.

Hence, such patients who respond readily to a sanatorium regime are allowed to remain at home, where they are inadequately treated and soon become moderately or far advanced. When the problem becomes acute, they are sent to a sanatorium.

If tuberculosis is to be successfully combated, children must be patch tested, those who react must be x-rayed, and *all* cases of tuberculous infection must be reported.

464 Commonwealth Avenue

MEDICAL PROGRESS

THE BILE PIGMENTS*

CECIL J. WATSON, M.D.†

MINNEAPOLIS

THE problem of the bile pigments has always been intriguing to the clinician as well as to the physiologist, pathologist and chemist. It is quite impossible to consider this problem adequately from any one of these viewpoints. The present communication, therefore, will strive to present a survey of recent general progress in this field, with particular emphasis, however, on clinical applications, and with some attempt to correlate or compare the results of recent studies with those of the older literature, at least sufficiently for purposes of orientation. The allotted space does not permit any comprehensive review of the literature, or even an inclusion of all the various aspects of the problem. The topic of the bile pigments in relation to hemoglobin metabolism must necessarily be omitted in large part, and greater emphasis is placed on the relation of the bile pigments to jaundice and liver disease.

BILIRUBIN

For many years, it was generally held that the transition of hemoglobin to bilirubin was characterized by a primary splitting off of the protein globin, with resulting formation of hematin. The next step was thought to be the removal of iron, followed by an opening of the porphyrin ring to yield bilirubin. This belief was founded to some extent on the ease with which hematin is obtained in vitro from hemoglobin, as well as on the known occurrence of hematin, under certain circumstances, in vivo; there was also the old idea that the iron-free hematoporphyrin of Hoppe-Seyler was an isomer and probable precursor of bilirubin. The latter investigations of the Hans Fischer school revealed clearly that the underlying porphyrin in the hemoglobin molecule, and the one standing in closest relation to bilirubin, is not hematoporphyrin but protoporphyrin. All these earlier beliefs have been dealt with in a previous review,¹ and need not be considered in more detail. Within the past few years, new concepts of bile-pigment formation have been introduced

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*From the Division of Internal Medicine, University of Minnesota Hospital.

†Professor of internal medicine, University of Minnesota Medical School.

that are based on the much firmer ground of an *in vitro* method of conversion of hemoglobin to bilirubin without the aid of living cells. Although it remains to be proved that this method obtains *in vivo*, there can be no doubt that it is sufficiently simple and physiologic in type to be quite compatible with an *in vivo* mechanism.

Perhaps the first observation bearing on this new concept was that of Fischer and Lindner² in 1926. They observed that green compounds, assumed to be similar to bile pigments, were formed when yeast and hemoglobin were incubated together. Warburg and Negelein³ observed that when hemin is treated with pyridine-O₂-hydrazin hydrochloride a "green hemin" results. This was studied further by Lemberg et al.⁴ who identified it as a biliverdin-iron-globin compound. By means of a coupled oxidation of hemoglobin or hemin with ascorbic acid, Lemberg and his co-workers⁵⁻⁹ obtained bile-pigment-iron-protein compounds designated as "choleoglobin," "verdo-hematin" or "verdohemochromogen." The first crystalline bilirubin was prepared by the same general procedure by Fischer and Libowitzky,¹⁰ although in this study an artificial coprohemin was used and an analogous coprobilirubin was isolated. The results, nevertheless, are just as significant so far as the underlying principle is concerned. This method of preparing bilirubin from hemoglobin *in vitro* has been confirmed by others.¹¹⁻¹³ The intermediary green compound differs from hemoglobin or hemin, as the case may be, through an opening of the protoporphyrin ring by an oxidative removal of the α -methene bridge. There is some reason to believe that the iron must be present for the porphyrin ring to open, at least under natural conditions. Thus, the administration of iron-free protoporphyrin to dogs with biliary renal fistulas was not followed by an increased excretion of bilirubin.¹⁴

It is probable that the so-called "pseudohemoglobin" of Barkan¹⁵ is closely related to Lemberg's verdohemoglobin. (As prepared *in vitro* by the action of hydrogen peroxide, the compound obtained, according to Lemberg,⁶ is actually a ferrous denatured globin-cyancholechromogen.) Barkan has shown that the iron of the pseudohemoglobin is "easily split off" by dilute hydrochloric acid, whereas that of ordinary hemoglobin is unaffected. The presence of a certain amount of easily-split-off iron in the hemoglobin of normally circulating erythrocytes indicates that at least a fraction of this hemoglobin is of the pseudohemoglobin or verdohemoglobin type.⁹ Barkan^{15, 16} has further shown that sterile incubation of erythrocytes for six hours is followed by an increase of

iron and bilirubin in the supernatant plasma, as well as pseudohemoglobin in the red cells. All this indicates an intracorpuseular degradation of hemoglobin. The magnitude of the total wastage of hemoglobin is unknown. Recent studies by Watson and Paine¹⁷ have shown that the erythrocytes sequestered in the splenic pulp and thrown into the splenic vein after adrenalin is administered, particularly in cases of hemolytic jaundice, are comparatively poor in hemoglobin. This reduction in hemoglobin concentration was unexplained except on the basis of intracorpuseular degradation during the period that the cells were in the spleen. The associated increased spheroidocytosis and increased fragility of the splenic-vein erythrocytes, noted after adrenalin, may be fundamentally correlated phenomena. Thus, Fahreus¹⁸ has shown that stasis of red cells in the spleen, or *in vitro*, results in increased spheroidicity, which he believes to be due to formation of lysolecithin as a result of the change in the interface relation between the red cells and the plasma. It is quite possible that all these phenomena are correlated with a reduction of catalase in the erythrocytes, which Engel^{12, 13} has shown to be of importance in retarding the conversion of hemoglobin to verdohemoglobin. Under ordinary circumstances, free hemoglobin in the plasma is quickly converted to bilirubin,¹ so that it is quite obvious that a relatively high degree of protection from oxidation obtains within the cells. Whether this is entirely due to catalase or not is unknown. This question is referred to below in the consideration of "pentdyopent."

In the conversion of hemoglobin to bilirubin, the fate of the globin is quite unknown. Duesberg^{19, 20} suggested that the globin is never separated and that the plasma bilirubin is in fact a bilirubinglobin. This possibility will be returned to shortly. It may be noted first that Duesberg's belief was based on his own and Bingold's²¹ observations that hematin, quite in contrast with hemoglobin, did not appear to be converted into bilirubin *in vivo*. A series of experiments* carried out in this laboratory have failed to confirm this belief and in fact have provided abundant evidence that the conversion of hematin to bilirubin is just as quantitative as that of hemoglobin.

Studies of the nature of the direct and indirect van den Bergh reactions have recently thrown much light on the general problem of bilirubin and the serum proteins. The earlier view that the indirect reacting bilirubin was attached to the serum globulin²² has been shown to be incorrect.

*Watson, C. J. *Pass. I*, and Schwartz, S. Unpublished data.

The studies of Bennhold,²³ Pedersen and Waldenstrom⁴ and Coolidge²⁰ clearly reveal that both direct and indirect types are bound to the serum albumin. Bennhold⁴ points out that if it were not for the attachment of bilirubin to the serum albumin, jaundice would undoubtedly be more intense than it is, since the concentration of bilirubin is regularly higher in the serum than in the tissues. The indirect reacting bilirubin, according to Coolidge,²⁰ is chemically bound (with valence bonds), whereas the prompt, direct reacting type is simply absorbed loosely.

If Duesberg's¹⁹⁻²⁰ hypothesis is correct, it follows that globin is closely akin to, if not identical with, serum albumin. Pedersen and Waldenstrom²¹ emphasize the close physical similarity, the main difference being in the isoelectric point of hemoglobin (pH, 7.0) and serum albumin (pH, 4.8). The two proteins have identical molecular weights and they are not separable in the ultracentrifuge.²⁴ It is at least obvious, at this stage of our knowledge of the problem, that the globin could well remain attached throughout the transition of hemoglobin to bilirubin, and could then be incorporated in the serum albumin fraction, still attached to bilirubin. In fact, this appears to be much more reasonable than to assume that the bilirubin and globin are separated only to have the bilirubin reattach itself to another and very similar protein. Here again, it is evident that further investigation is needed.

From the foregoing statements, it should not be assumed that the different mechanism of the indirect, as compared with the prompt direct van den Bergh reaction, has been proved to depend on the type of attachment to serum albumin. It appears that this is important, but it remains to be shown that purely chemical differences in the bilirubin molecule are not also of significance. The question of furan ring formation, as suggested by Fowweather,²⁰ was considered at some length in an earlier review.¹ The most recent studies of the Fischer²⁷ school indicate the presence of a furan ring in the molecule. Davis and Sheard²⁸ have shown that a distinct difference exists in the ultraviolet absorption spectrums of the prompt direct and the indirect reacting types of bilirubin. Previous studies had indicated another physicochemical difference between the two types—that is, a difference in filtrability through semipermeable membranes. Recent studies by Gregory and Andersch²⁹ failed to confirm this supposed difference. Snapper and Bendien³⁰ have shown, however, that *in vitro* studies of the ultrafiltrability of bilirubin are rendered difficult of interpretation because of a number of variable experimental factors. Heilbrun and Hubbard³¹ have recently called attention again to

the chloroform solubility of the indirect reacting bilirubin in the serum. They recommend simple repeated extractions of the serum with chloroform, which is separated by centrifuging and is then compared with a standard potassium bichromate solution. This appears to be a useful procedure, especially when a photoelectric colorimeter is not available for employment of the Malloy-Evelyn³² method.

Another interesting theory regarding the basis of the different diazo reactions has been suggested by Colangiuli³³ mesobilirubin is responsible for the delayed or indirect reaction, bilirubin only for the prompt direct. This assumption merits further study. Mesobilirubin is intermediary between bilirubin and mesobilirubinogen, the latter being one of the urobilinogens. Mesobilirubin is lighter in color than bilirubin (yellow rather than orange) but in other respects behaves like it, giving the Gmelin color play with yellow nitric acid, as well as the diazo reaction, but not Ehrlich's aldehyde test. The occurrence of mesobilirubin in nature has not yet been proved. It is readily prepared from bilirubin by suitable reduction, and it is entirely conceivable that bilirubin might be reduced in part either in the blood stream or in the organs with resultant mesobilirubin formation. It has been shown, for example, that crystalline stercobilin injected intravenously is often reduced in part to stercobilinogen.¹

The determination of serum bilirubin has become much simpler and more accurate because of the adaptation of the van den Bergh method to the Evelyn photoelectric colorimeter. The procedure described by Malloy and Evelyn³² permits ready distinction of the direct and indirect reacting serum bilirubin. Unfortunately, however, they recommend reading the total direct reacting bilirubin only after thirty minutes. This, of course, combines the prompt and delayed types, which have entirely different significance. In the laboratory of the University of Minnesota Hospital, it has been customary for some time to take readings at one minute and again at fifteen minutes, the first being the prompt reacting bilirubin and the second the delayed type. The total is then determined by the Malloy-Evelyn method, the difference between this and the amount observed at fifteen minutes constituting the indirect fraction. The original van den Bergh method and many subsequent modifications of it undoubtedly gave low values for total bilirubin because of some loss on the protein precipitated by the alcohol. Malloy and Evelyn³² found that the indirect reaction was just as complete with 50 per cent or even lower concentrations of alcohol and that the serum pro-

teins were not precipitated at this concentration if the serum was first diluted. The sensitivity of the Evelyn colorimeter is quite sufficient to permit this dilution.

The bilirubin tolerance test of liver function, as originally described by von Bergmann and Eilbott, was the subject of a critical study by Strasser,³⁴ who concluded that the method affords a very delicate means of testing the bilirubin excretory function of the liver in nonjaundiced persons. More recently, Weech and his associates³⁵ have suggested a bilirubin clearance test applicable as well to jaundiced patients, the rate of removal being evaluated as a velocity constant of excretion, a measure that these investigators believe to be unaffected by elevation of the basal plasma bilirubin concentration.

BILIRUBIN DERIVATIVES OF CLINICAL IMPORTANCE

Biliverdin

This substance, also known as dehydrobilirubin because it is formed by dehydrogenation of bilirubin, comprises the pigment fraction of verdohemoglobin, as noted above. There is no reason to believe, however, that biliverdin as such is contributed to the serum from destroyed hemoglobin. If this were true, accumulation of biliverdin—in other words “biliverdin icterus”—might be expected in cases of retention jaundice, especially those of hemolytic type. The occurrence of biliverdin in the serum has been studied recently in this laboratory.* With the Evelyn photoelectric colorimeter, the serum biliverdin is readily determined by virtue of its relatively strong absorption in the red portion of the spectrum. This study is not completed, but the results so far obtained indicate that biliverdin does not accumulate in pure retention jaundice. In regurgitation jaundice, whatever the cause, some biliverdin has been noted regularly. Except in jaundice due to cancer, however, the serum biliverdin has not exceeded 1.0 mg. per 100 cc., in accord with the observation that outspoken biliverdin jaundice is most frequently due to cancer of the biliary tract.³⁶ A few marked exceptions have been noted in which the jaundice was of parenchymal type (subacute or prolonged hepatitis or cirrhosis).

A “green reaction” with Ehrlich’s test for urobilinogen in the urine is encountered in some patients with marked bilirubinuria. This has been shown to be due to biliverdin formed by the action of sufficiently high nitrite concentration in the urine, and stabilized at the biliverdin stage by the *p*-dimethylaminobenzaldehyde of the reagent.³⁷

*Watson, C. J., and Larson, E. Unpublished data.

Urobilinogens and Related Compounds

Historical facts. In a consideration of recent advances in the study of this group, it is desirable for purposes of orientation to refer briefly to some of the earlier literature. The term “urobilin” was first employed by Jaffe³⁸ in 1866 to describe an orange pigment, which he observed both in bile and in certain urines. Jaffe noted that this substance exhibited intense green fluorescence with zinc chloride and ammonia, as well as a strong absorption band in the region of 500 millimicrons. In 1871, Vanlair and Masius³⁹ found an entirely similar pigment in the feces. With appropriate caution, since they were uncertain of its identity with Jaffe’s urobilin, they designated the fecal pigment as stercobilin. The description of these substances was confirmed, in the main, by MacMunn⁴⁰ in 1878. It must be noted, however, that MacMunn described a distinct, although slight, difference in position of the absorption band of the urobilin from bile as compared with that from urine. In 1901, Ehrlich⁴¹ described a color reaction in the urine with concentrated hydrochloric acid and *p*-dimethylaminobenzaldehyde. Although he was ignorant of the substance giving this reaction, he was aware that it was relatively common in cases of liver disease and in certain anemias. Neubauer⁴² was the first to show that the reaction was due to the presence of a chromogen of Jaffe’s urobilin. This chromogen was further studied by le Nobel,⁴³ who named it “urobilinogen.” As early as 1887, Friedrich von Müller⁴⁴ had shown that the formation of urobilin and its occurrence in the urine were dependent on the presence of bile in the intestinal tract, thus demonstrating simultaneously the enterogenous origin of urobilin and its enterohepatic circulation. This work was confirmed many years later by the extensive studies of McMaster and Elman.⁴⁵ The first concrete knowledge of the chemistry of this group of substances was provided by Fischer⁴⁶ in 1911. He reduced bilirubin with amalgam, and then isolated the resulting chromogen in crystalline form.⁴⁶ This was first designated as “hemibilirubin,” since the yield was less than 50 per cent and it was thought that but half the bilirubin molecule had been converted into the crystalline chromogen. In the same year, the substance was isolated from urines rich in urobilinogen (strong Ehrlich reaction).⁴⁷ By 1914, Fischer⁴⁸ had shown that mesobilirubin was intermediary and that there was no evidence that half the bilirubin molecule was converted to some other compound during the reduction. The chromogen was therefore renamed “mesobilirubinogen.” On exposure to light and air, this substance develops urobilin characteristics, and the Ehrlich

reaction gradually disappears. The transition can be hastened by mild oxidizing agents, such as iodine. This was employed by Schlesinger,⁴⁹ together with alcoholic zinc acetate, in what has become the best known qualitative test for urobilin (not urobilinogen).

Recent fundamental advances. For a number of years after the studies of the Fischer school, the question whether mesobilirubinogen was the sole urobilinogen remained unanswered. Was the stercobilin of the feces identical with the urobilin derived in vitro from mesobilirubinogen? Prior to 1932, many attempts^{40, 50-52} to answer this question by isolating either chromogen or pigment from the feces had failed. In 1932, crystalline stercobilin was isolated from human feces.^{53, 54} The same substance was obtained from pathologic human urines in 1933.^{55, 56} A method was then devised for preparing crystalline urobilin from mesobilirubinogen, and it was shown that this urobilin differed in a number of respects from stercobilin.^{57, 58} This was confirmed by Fischer and his co-workers.⁵⁹⁻⁶¹ Siedel and Meier⁶¹ synthesized this compound and designated it as urobilin IX *a*, indicating simply that the configuration corresponds with that of the protoporphyrin in the hemoglobin molecule—that is, Type IX of the fifteen possible isomers—and also that the porphyrin ring has opened at the α -methene bridge. Fischer and his associates⁵⁹ found that although urobilin IX *a* is optically inactive, stercobilin is strongly levorotatory. This will be referred to again in the following. They also noted that the melting points of the free substances were distinctive when recrystallized from acetone.^{60, 61} Shortly after the isolation of stercobilin, attempts were made to reduce it and isolate the chromogen to determine whether or not this was mesobilirubinogen. The reduction is easily carried out, but the resulting chromogen (stercobilinogen) has not yet been crystallized, although mesobilirubinogen crystallizes readily in much smaller amounts under the same conditions. Recent studies have to some extent clarified the nature of stercobilin and its relation to mesobilirubinogen.

The possibility that there were two bilirubins in the bile—one on reduction in the intestinal tract yielding mesobilirubinogen and the other stercobilinogen—was first considered. It was quite conceivable, for example, that some of the porphyrin of the hemoglobin molecule might open its ring, not at the α -methene bridge, but at one of the other three. This, of course, would result in the formation of a different bilirubin, or a bilirubinoid substance. With this in mind, a number of human bile samples were reduced directly with

amalgam, until the Ehrlich reaction had become strong.⁶² The resulting urobilinogen, after partial purification, was converted to urobilin, which was then isolated. In every sample, this was urobilin IX *a* on the basis of optical activity, absorption spectrum and melting points. Stercobilin was never formed in this way, although it was occasionally native* in the bile, in which event it was first removed. This study revealed conclusively that the formation of stercobilin is dependent on a more complex sequence of events than the simple reduction of the bilirubin present in the bile. Lemberg⁶³ recently recommended that the term "stercobilin" be abandoned, but in view of these findings and other observations, which will be mentioned, it appears that the term is more descriptive than any other, since it is now certain that stercobilin formation is dependent on a peculiar chemical activity in the intestinal tract, probably related intimately to bacterial metabolism in the colon.

Experiments were next carried out with the specific purpose of determining whether stercobilin is derived from mesobilirubinogen. The possibility existed, of course, that it might be an offshoot from any of the intermediary reduction compounds in the pathway from bilirubin to mesobilirubinogen, such as mesobilirubin and dihydromesobilirubin. It was found that if crystalline mesobilirubinogen was given by mouth this was followed by an increased output of stercobilin in the feces.⁶⁴ Incubation of mesobilirubinogen with normal feces resulted in a clear-cut increase of stercobilin.⁶⁴ This was not true, however, of strictly acholic feces, in which mesobilirubinogen was unchanged. The addition of bile to such samples caused stercobilin formation in some, whereas a type of urobilin that is regularly observed in infected bile samples appeared in others. This new or third urobilin, as described by Schwartz and Watson,⁶⁵ is of particular interest in that it is dextrorotatory in the same magnitude that stercobilin is levorotatory. The melting point is the same as that of stercobilin, but the absorption is identical with that of urobilin IX *a*. The first two characteristics suggest that *d*-urobilin, as this substance has been designated tentatively, may be a stereoisomer of stercobilin. Further studies of this question are planned. Dextro-urobilin is further characterized by a color play with dioxan hydrochloric acid.⁶⁵ A slight difference in the absorption maximums of urobilin IX *a* and stercobilin was first reported by Lemberg,⁶⁶ although the former had not at that time been crystallized or identified as

*The presence of stercobilin in the bile may be ascribed without doubt to the enterohepatic circulation. Crystalline stercobilin, when injected intravenously, reappears in the bile unchanged.

a distinct entity. Dextro-urobilin may usually be obtained from infected human fistula bile, although the yields are small owing to the difficulty of purification. Schwartz, Sborov and Watson⁶⁷ have further noted that mesobilirubinogen added to such infected samples is at least partially converted to *d*-urobilin. The significance of this change, as compared with that to stercobilin in normal feces, is as yet unknown. The above-mentioned experiments with acholic feces, bile and mesobilirubinogen, in which on one occasion stercobilin and on another *d*-urobilin were formed, indicate that some unknown factor influences the direction of the conversion. It is also un-

known whether there is a separate chromogen for *d*-urobilin as there certainly is for stercobilin, or whether mesobilirubinogen, under proper conditions, is converted directly to the dextrorotatory compound. As yet, no clinical importance has attached to this substance. It is quite conceivable that it will be found in the urine in biliary-tract infections, since it is well known that urobilin may be formed in the infected biliary tract.⁴⁵ It would also be of interest to investigate the bile obtained by duodenal drainage, with respect to the presence of *d*-urobilin. There can now be little doubt that the slight spectroscopic difference recorded for bile urobilin by MacMunn,⁴⁰ in 1878, was due to the presence of *d*-urobilin.

Thus, the quantitative determination of urobilinogen in the urine and feces includes any or all of the chromogens present in the sample. It has been shown repeatedly that both stercobilinogen and mesobilirubinogen occur in the feces and urine.¹ There is no evidence at present that either of these substances has a different clinical significance

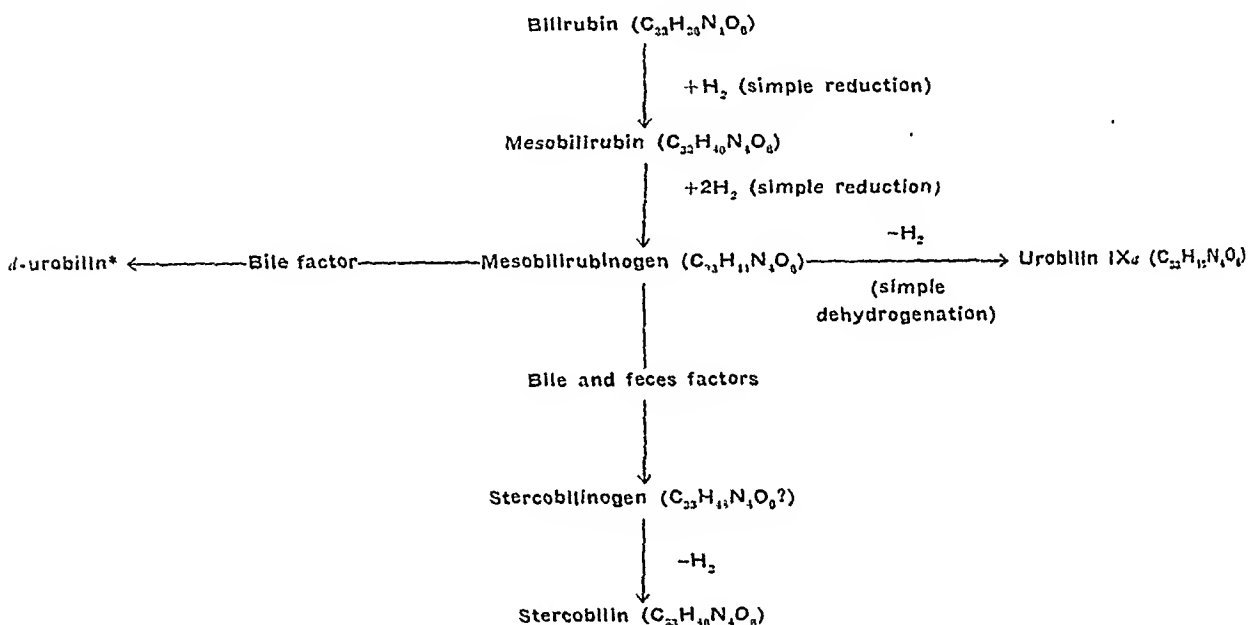


FIGURE 1.

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As a result of these studies, it is evident that urobilinogen as tested for by the Ehrlich reaction

*As yet there have been no elementary analyses of this substance, so that the empirical formula is unknown.

from the other. Lemberg⁶⁸ suggested such a possibility on the basis of a differential test for stercobilin and urobilin IX *a* that was applicable to urine extracts. He found that heating with iron chloride and hydrochloric acid produced a violet reaction with urobilin IX *a*, whereas stercobilin was unchanged. When this method was applied to urine samples from various diseases, stercobilin was regularly found, and urobilin IX *a* but rarely. Lemberg therefore suggested that the latter might be pathologic. On the other hand, mesobilirubinogen (the precursor of urobilin IX *a*) has been isolated from the urine in considerable amount in widely divergent conditions, such as hepatic cirrhosis and other diseases,^{46, 48} including hemolytic jaundice.⁶⁸ In hemolytic jaundice, stercobilin was obtained from the mother liquor in an amount of the same magnitude as that of the mesobilirubinogen. In

a consideration of Lemberg's suggestion, the question must be taken into account of the relative amount of stercobilinogen formed in the colon as compared with that of unchanged mesobilirubinogen. Exact evidence on this point is lacking. Nevertheless, it will be seen in Figure 1 that when bile is entering the intestinal tract, the factors are present for the conversion of mesobilirubinogen to stercobilinogen. Quite in accord with this belief, it has been noted during numerous isolations of crystalline stercobilin from various samples of feces, that this substance appears to predominate in amount over the remaining fraction of the urobilin that is not crystallized (some of which is probably urobilin IX *a*). It is true that a comparison of amount is rendered somewhat difficult because mesobilirubinogen and urobilin IX *a* are not so stable as stercobilinogen or stercobilin and that they are converted in part to mesobiliviolin during the isolation procedure.^{6,7,10} In spite of this, it is believed that the majority of the bilirubin of the bile is eventually excreted in the feces as stercobilinogen and that any marked preponderance of mesobilirubinogen in a given urine sample indicates either an unusually rapid absorption of mesobilinogen from the right colon or an altered chemical activity in the colon—for example, diminution of the factors necessary for the conversion of mesobilirubinogen to stercobilinogen.

(To be concluded)

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NEW HAMPSHIRE MEDICAL SOCIETY

. PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-FIRST ANNUAL MEETING

May 12 and 13, 1942

TUESDAY, MAY 12

THE scientific session of the New Hampshire Medical Society was opened at the Hotel Carpenter, Manchester, at eleven-thirty o'clock in the morning, with President Charles H. Dolloff presiding.

Dr. Deering G. Smith made the following remarks on the Procurement and Assignment Service.

I want to thank the members of the Society, especially the members of the county and state Medical Preparedness and Procurement and Assignment Committee, for the excellent work they have been doing. I expect that this co-operation and work will continue.

The Procurement and Assignment Service has been established to decide which doctors will go into the Army or Navy and which doctors will be considered essential for the care of the civilian population. In other words, at the same time the Army needs are taken care of, sufficient doctors must be kept at home to take care of civilian needs.

It has been stated that the Selective Service System is the dogcatcher, and the Procurement and Assignment Service is the Society for the Prevention of Cruelty to Animals.

In this state, the organization is headed by myself, as chairman; serving on the committee are Drs. Jones, of Manchester, and Bowler, of Hanover. In each county, there is a similar committee to advise the state committee.

Medical-enrollment forms have been sent to each doctor, and should be filled out and returned to the proper authority at once. If any of the doctors have not received these blanks, I shall be glad to furnish one.

Most of the doctors in the state have been classified as 3A under the Selective Service System. General Bowen, head of the Selective Service System in New Hampshire, has received instructions, which he is sending to the local boards today or tomorrow, notifying them to reclassify the doctors who are now in 3A. In the reclassification, the amount these doctors will receive as commissioned officers in the Army and Navy will be considered in figuring out whether or not they have dependents in sufficient number so that they will have to stay at home, rather than go into the Army.

The belief is that practically every doctor will be reclassified from 3A to 1A. He will be given a reasonable

time to apply for a commission in the Army if he is not considered essential, and will then, if he does not apply for a commission, be inducted as a private.

The need for medical officers is 15,000 more in 1942, and 5000 before July 1. That breaks down to 50 the number of medical officers needed in New Hampshire before July 1. To assist in the securing of this quota, the National Recruiting Board has established a medical recruiting board in New Hampshire. That is headed by Captain Weimars, of the Medical Corps. It gives me pleasure to introduce Captain Weimars.

Captain Weimars spoke as follows:

The Medical Officers' Recruiting Board will probably be located at 77 Main Street, Nashua. The purpose of this organization, as Dr. Smith has pointed out, is to get medical officers for the Army. He has told you how many are needed—about 5000 from the United States to be obtained before July 1. And, of course, an applicant must be physically fit before he can be given a commission.

We have the authority to cut the red tape, or at least to make it as light as possible, to get medical officers into the Army. We have the authority to act for the Surgeon General. We have the authority to disqualify or qualify physically any applicant for medical duty.

If you have been reading the *Journal of the American Medical Association*, you will have noted that the physical qualifications for medical officers have been considerably reduced. We have now what is termed a limited service. The limited service covers everything but field duty. Probably, such men will not see foreign duty. Thus, we can waive certain physical defects, such as missing teeth, an insufficient number of teeth, carious teeth and other minor defects.

An applicant must be a licensed practitioner of the State, must have had one year's internship, must be a citizen of the United States, and must be between the ages of twenty-six and forty-five. We can offer commissions to any person under thirty-seven to rank as a first lieutenant. We are authorized to recruit and commission applicants as first lieutenants, unless they have special qualifications, are members of a specialty Board or fellows of the American College of Surgeons or the American College of Physicians.

However, we have the authority, if applicants over thirty-seven and under forty-five meet certain qualifications, to commission them as captains.

A first lieutenant, unmarried and without dependents, gets approximately \$2700 a year. A first lieutenant, married, or having dependents, gets approximately \$3100 a year. A captain, unmarried, gets \$3300 a year, and a captain, married, gets \$3800 a year.

We have on our medical recruiting board a member from the Office of the Adjutant General who has the authority to swear in an applicant and give him his commission, serial number and rank and have him ready for active duty within a very short time. Accordingly, I present to you Lieutenant Veagle.

Lieutenant Veagle spoke as follows:

The Army needs medical officers. That is naturally true because a good many of your fellow citizens have been taken into the armed forces; consequently, some of you will have to go along with them to help protect them and keep them in good health and bring them back again. This program is being speeded up. Heretofore to obtain a commission, it took weeks and months and a good deal of red tape, the necessary papers were incomplete or lost here and there in Washington. When we once start to operate, a physician probably will be able to obtain a commission within a week at the most. Of course you will be allowed fourteen days after you receive your commission, or are sworn in, and under certain conditions you will be allowed a greater length of time. If you wish to waive the fourteen days and immediately go on duty undoubtedly we can find an assignment for you within a few hours.

Dr Metcalf read the following letter from the Bureau of Narcotics at Boston:

I deem it necessary to bring to the attention of the officers of the New Hampshire Medical Society information that should be disseminated for the protection of its members.

About this time of year, numerous carnivals, circus companies and outdoor shows start their season and visit various cities and towns throughout the State. This bureau has learned from experience that some of the personnel of these groups and their followers are frequently drug addicts. To obtain narcotics for the satisfaction of their addiction, these persons approach physicians in the towns where they are appearing, usually with a convincing story of an ailment that requires morphine for relief or even a story that they are on the way to a sanatorium for treatment and need a certain amount to tide them over. Physicians cannot be too careful about being prevailed on by these people, who have no medical need for narcotics.

I strongly urge the members of your society to be on their guard against the danger of being imposed on by such addicts. Unfortunately, the New Hampshire state law is inadequate in its provisions for prosecution of addicts who obtain narcotics, for the satisfaction of their addiction, under pretense, and the federal law has no punishment for the addict. However, under the federal law, any physician who prescribes or dispenses drugs indiscriminately, other than for an established medical need, is subject to prosecution for violation of the Harrison Narcotic Act, as amended. Every physician is required to determine, from a personal examination of a patient, that patient's medical need for narcotic drugs before prescribing or dispensing same. A physician should never accept the word of a patient that he has a certain physical ailment and requires narcotics for relief, or that a physician in another city has been giving him prescriptions for a

certain amount. You are cautioned to exercise extreme care to prescribe and dispense narcotics in the course of your professional practice only, and to patients under your care whose medical need has been definitely established by yourself.

In these days when careful conservation of the supply of narcotic drugs on hand is necessary because of world conditions, the Bureau of Narcotics is confident that the medical profession will co-operate wholeheartedly to prevent any diversion of these drugs to illegitimate channels.

WM E CLARK, District Supervisor

The morning session was concluded with an address by Dr Paul D White, of Boston, who opened the symposium on heart disease with a paper entitled 'Important Clues in Cardiovascular Diagnosis.'

The afternoon session convened at two o'clock with President Dolloff presiding.

Dr Ashton Graybiel, of Boston, continued the symposium on heart disease with a paper, entitled 'Electrocardiography.' Dr Richard Schatzki, of Boston, concluded the symposium with an address, 'Cardiovascular X-ray.'

Dr Bertrice M Kesten, of New York City, then presented a paper, entitled 'Dermatology.' The afternoon session was concluded with a talking, motion picture film in color, entitled 'Sex Hormones: Physiology, diagnosis and therapy,' which was presented by Parke, Davis and Company.

WEDNESDAY, MAY 13

The morning session convened at eleven fifteen o'clock, with President Dolloff presiding.

The following remarks were made by the visiting delegates from other New England state medical societies:

DR CARL E RICHARDS, Alfred, Maine: It gives me great pleasure to be able to attend this annual meeting of the New Hampshire Medical Society, and to be able to extend the greetings of the Maine Medical Association to you. I have enjoyed the meeting very much up to this point and I think the papers and discussion groups have been above par.

Being a general practitioner, I was particularly impressed with the papers presented yesterday in the symposium on heart disease and the paper on dermatology by Dr Kesten.

I am looking forward to hearing the papers by Drs Irons, Adair and Barker, and also to the banquet tonight, which I believe is a standing event.

The annual meeting of the Maine Medical Association will be held at the Poland Spring House, Poland Spring, Maine, on June 21, 22 and 23, and I have been asked by the president of the association to extend an invitation to the members of the New Hampshire Medical Society. The way things are with gasoline and tires and the like, we believe that this may be one of our last large meetings for the duration and an outstanding program has therefore been arranged, which will be brought to a conclusion by the appearance of Dr Morris Fishbein at the annual banquet on Tuesday evening, June 23.

DR. BERTRAND F. ANDREWS, Middlebury, Vermont: I was able to attend your meeting only today, so that I have not been here throughout the whole meeting. However, I am very glad to be able to be here with you and to bring you the greetings of the Vermont State Medical Society.

DR. C. BERTRAM GAY, Fitchburg, Massachusetts: I am very glad to be with you, and to bring the greetings of the Massachusetts Medical Society, as well as greetings from our president, Dr. Ober.

I came in a little while ago, and I see that you have a very interesting gathering here. Earlier this morning, I attended the Surgical Section, and heard a good discussion of gall-bladder disease.

We invite you to be with us at our annual meeting in Boston at the Hotel Statler in two weeks.

DR. JOHN J. CURLEY, Leominster, Massachusetts: I think that Dr. Gay has expressed the thoughts of the Massachusetts Medical Society very well.

DR. PAUL R. FELT, Middletown, Connecticut: By way of a long-continued and friendly tradition, I extend to you the greetings of the Connecticut State Medical Society. I can even say that after an abominable bus ride from Middletown to Manchester! We cordially invite all of you to the annual meeting of the Connecticut State Medical Society in Middletown the first week in June—I am not exactly sure of the dates at the moment. Our meetings will be held on the campus of Wesleyan University, and we are planning a very enjoyable time and shall be glad to see you there.

Dr. Ernest E. Irons, secretary of the Board of Trustees of the American Medical Association, presented the first paper of the morning, entitled "Aspiration Pneumonia." This concluded the morning session.

The afternoon session convened at two o'clock, with President Dolloff presiding.

Dr. Zatae L. Straw, of Manchester, was awarded a fifty-year-membership gold medal, and spoke as follows:

I thank you very sincerely for this signal honor, which you have conferred on me today in giving me this medal as a token of fifty years of busy, interesting and, I hope, worthy service in the practice of medicine in New Hampshire.

Of course, my being here is due to two factors only. One is the magnificent health I inherited from a long line of stalwart ancestors; the other is a determined and, I might say, congenital vocation to study medicine, because in my immediate family there were for years eight practicing doctors, although at present there are only five in three different states—New Jersey, Pennsylvania and New Hampshire.

I know the secret of popular public speaking. This is the recipe, which I intend to follow: be brief; be sincere; be seated. I shall not detain you for more than a moment, nor am I going to subject you to any résumé of the wonderful progress in the medical field during these fifty years. But I must refer, briefly, to the fact that, when I began to practice, we did not have sulfanilamide or the wonderful group of derivatives in that family. We did not know anything about insulin, through which years of comfort and active life are added to an otherwise hopeless outlook, or plastic and orthopedic

surgery and the wonder-working feats that are performed today, through which mangled and hopeless wrecks of humanity are transformed into active citizens. We had none of the modern anesthetists and the agents that they work with. We had practically no antiseptics or asepsis to speak of, as compared with what we have today. We knew nothing about blood transfusions or serum therapy. We did not know much of anything, some of you younger chaps will think, but we got along, and sometimes our patients got well. We are grateful. Once in a while they paid us, and that was a help, too, even then. If they did, it was all right, because that old doctor was not only the physician but also the legal adviser and minister and friend and moneylender and a good neighbor in every sense of the word.

Nowadays, we have no time for that. But that is the way it used to be.

We hope for much better things. However, in the next fifty years, I cannot possibly foresee such great progress in this or any other field as we have experienced in the last fifty years.

It has been a great treat, a great boon, to have lived in these fifty years, and I doubt if the next hundred years will hold as much interest and progress in any line.

Fifty years ago, the woman doctor was an unknown quantity, more or less, a rare species. They hardly knew how to take us. But, I joined the medical society, and since that time I have been accepted and treated just like one of you, and that is precisely as I wanted to have it. I have had a square deal in every way, and I want to express my appreciation and gratitude to the boys in Manchester, to my associates in the medical profession in Manchester, for their unvarying courtesy and friendly, professional consideration during all these years.

Another fifty-year-membership gold medal was awarded to Dr. Edwin P. Hodgdon, of Lakeport, who spoke as follows:

I thank the members of the New Hampshire Medical Society for this wonderful emblem. I never really expected to receive one, because twenty-five years ago, I was refused life insurance by a well-known company because of my family history and also because of a large abdominal girth. However, I served notice on the Chief Medical Examiner that I would be present at his funeral!

There is an old saying that the first fifty years are the hardest, but I want to rebut that statement: I can truthfully say that the first fifty years have been grateful ones to me. In the "Gay Nineties" I think I enjoyed myself as much or more than I have in the following years. We did not have tire or gasoline troubles. The only thing we had to find out was the price of plain oats.

Dr. H. O. Smith then made the following remarks:

In September, 1859, a baby boy appeared in the town of Milford, and his parents burdened him with the long name of Herbert Stillman Hutchinson. The boy waxed in stature and in wisdom. In due time, he entered Dartmouth. He graduated from Dartmouth in the year 1875, sixty-five long years ago. Today, he is the oldest in the list of living Dartmouth graduates.

After graduation, he began the study of medicine. He went to Bellevue Hospital Medical College, which did itself honor by giving him the degree of M.D. in 1880.

After his graduation, he returned to his home town of Milford, and he has been practicing medicine there ever

since. He is known and loved by every man, woman and child in that town.

Ten years ago, we gave Dr. Hutchinson a gold medal representing his fifty years of membership in the Society. Today, he has attained the rare distinction of having been a member for sixty years.

Mr. President and members of the Society, I deem it a great honor and a great privilege to present to you Dr. Herbert Sullman Hutchinson, our sixty year member.

Dr. Hutchinson spoke as follows:

It was a considerable surprise to me when I was asked to be here today. I had supposed that my presence was no longer needed.

The two members of the Society who have preceded me and I belong to what is known as the horse and buggy days and that means more to us, perhaps, than to those who have gone into the service more recently, bad roads, and more nightwork than is now indulged in. I mean muddy roads and ruts, spring and fall, and deep snows and unbroken roads in the wintertime. It meant everything that was exhausting to a person, if he so willed to take up the duties that he was called on to perform.

Since then, many things have happened. Many have passed on. The country doctor no longer has such a hard time in getting from one place to another. The automobile and better roads have revolutionized in a great measure the hardships that we formerly experienced.

After four years in the practice of medicine in Francestown, New Hampshire, I moved to Milford for several reasons. One was that the work was so hard that I could not stand it. I was quite rugged, too. The other was that my father, the owner of a great farm on which I was born and brought up, was very ill, and I thought that it was my duty to be where I could help him. I am getting along in years and most of my friends and associates and co-workers in medicine and surgery have passed on.

An eminent lawyer in a neighboring town said to me one day, "Doctor, ever since I was fifty years old, I feel that I have been occupying most of my time burying my friends. And that really occurs to me very often. Although the life span has increased and people live to be older, there are just as many dying as ever did but this comes in the old age variety of disease, which makes it a rather hopeless task to attempt to effect a lasting cure."

Medicine is hard work. We meet much prejudice and we meet people with set ways, who are unwilling, some times to abandon their notions of remedies and to follow our desired prescriptions. But we keep busy, and that is the answer to it all.

Being somewhat aged myself, I am now pretty well able to experience some of the symptoms that our patients display, and to know whether or not they are telling the truth. It is a human frailty to exaggerate sometimes and to misrepresent intentionally or otherwise, the symptoms as well as to minimize them, and to refuse to follow set directions, and that constitutes one of the hardest obstacles in the practice of medicine. If a person will not cooperate it makes an incomplete piece of work, and our work is hard enough as it is, without these obstacles.

An ex-president of the Society, not many months ago, made this remark to me, "Doctor, do you realize the difference in the preparation of the graduate from the medical school of today and what it was when you were graduated?" I said to him, "My dear man, I have recognized that every moment of my life. We did not have

the facilities presented to us to round out our courses and make things easy that are presented today. And, today, not only are they presented free but they are required. That is true in obstetrics, and it is true in surgical technique and various other things, and it is a great advantage.

And my ex-president friend continued, "When the doctors nowadays start out, they are several laps ahead of you fellows when you started. Do you realize that?" And I said, "I certainly do. It keeps me busy reading and studying and trying to keep abreast of the times. But it is work, and it is work that I love and that I shall follow so long as I have the strength to do so. There is no better remedy for the blues or for discouragement than hard work. Since this is my chosen occupation in life, it will follow with me to the end."

Major Weir, in the absence of General Bowen spoke as follows:

General Bowen called me up a short time ago, informing that he could not come here, but he did want me to express to the members of the Society his sincere thanks for the co-operation shown to him during the past year. He said that without that co-operation the Selective Service System could not have functioned at all smoothly, and from my own point of view, I want to thank all the physicians of the Society who have been in selective service work for their co-operation with me.

I think we can say that the record of the Society is unimpaired, in that I do not believe there has been any resignation from the system except for illness, or moving out of the State.

Secretary Metcalf then read the following resolution concerning the resignation of Dr. Henry O. Smith as a trustee:

WHEREAS, the House of Delegates learns with regret of Dr. Henry O. Smith's desire to retire from the Board of Trustees,

THEREFORE BE IT RESOLVED, That the House express to Dr. Smith its deep appreciation of his outstanding service to the New Hampshire Medical Society in the promotion of its best interest through his wise counsel and active participation in all its affairs during the many years of his membership.

Dr. Metcalf continued as follows:

The House of Delegates directed the Committee on Child Health to co-operate with the appropriate state and federal agencies to immunize, against diphtheria and smallpox, all children over nine months of age.

It awarded \$50 to the Cancer Committee to carry on its work for the coming year.

It decided to be a cosponsor in the New England Health Institute, which meets in New Hampshire in 1943. Details of this co-operation were left to the Committee on Public Health.

It accepted a bill concerning medical service corporations drawn up by Mr. Sulloway, and directed me to submit it to the Committee on Public Relations, who will submit it to the Legislature next year for their consideration.

The House of Delegates decided to co-operate with the National Physicians Committee, and it requests the members of each county society to contribute \$1.00 apiece. The Committee on Public Relations is to co-operate with the

National Physicians' Committee, the county secretary to turn the money over to the Treasurer, to be forwarded. That is for the expenses of the National Physicians' Committee.

It directed the Committee on Public Health to co-operate with the State Board of Health, to determine the minimum requirements for first-aid rooms in industry.

It directed me to write to our senators and representatives about a bill in Washington that would permit osteopaths to serve in the United States Army hospitals.

It directed me to notify Congress that they were opposed to a change in Section I of the Revenue Laws, which would permit the taxation of charitable and educational institutions.

It decided to cover the cost of the Procurement and Assignment Service from the general funds of the Society, so that we may run that service and not have it run by a federal agency.

It decided that residence in New Hampshire is not necessary for membership in the Society. Two or three men who formerly lived here and who now live outside the State wish to continue as members.

The House of Delegates decided to come to Manchester again in 1943. The meeting will presumably be held on May 11 and 12. You will be glad to know that I have already started to work on the 1943 program.

Your new vice-president is Dr. James W. Jamson, of Concord. Your new president is Dr. Timothy F. Rock, of Nashua. Dr. Sanders, of Claremont, was elected vice-president last year, and would naturally have moved up to the presidency. He said that he was unable to carry on the work of the presidency, so that Dr. Rock was elected in his place.

Dr. H. O. Smith then presented the report of the Trustees.

FINANCIAL REPORT OF THE TRUSTEES OF THE NEW HAMPSHIRE MEDICAL SOCIETY FOR THE YEAR ENDING JANUARY 1, 1942

Receipts

Interests on various deposits, other than Benevolence Fund	\$317.12
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Expenditures

Expenses of meeting (Sesquicentennial) 1941	1,000.00
Pray and Burnham prizes	100.00
Total expenditures	1,100.00
Decrease in funds, other than Benevolence Fund	782.78

GENERAL FUND	
Deposits. New Hampshire Savings Bank	\$4,859.13
Portsmouth Trust and Guarantee Company	2,005.46
Nashua Trust Company	205.18
United States Defense Bonds, Series "G"	3,000.00
Total funds available on January 1, 1942	\$10,069.77

BARILETT FUND	
Deposit: Portsmouth Savings Bank (\$352.11 of this is a permanent fund, the income to be "expended only for the benefit of medical science, as may be directed by vote of this society")	\$2,718.19
United States Defense Bonds, Series "G"	2,000.00
Total funds	\$4,718.19

PRAY FUND	
Deposit: Strafford Savings Bank (\$1000 of this is a permanent fund, the income to be expended only for prize essays)	\$217.41
United States Defense Bonds, Series "G"	1,000.00
Total	\$1,217.41

BURNHAM FUND	
Deposit: New Hampshire Savings Bank (\$1140 of this is a permanent fund, the income to be expended only for prize essays)	\$1,237.32
United States Defense Bonds, Series "G"	1,000.00
Total	\$2,237.32

BENEVOLENCE FUND	
Deposit: New Hampshire Savings Bank (\$394.50 of this is accrued income available for the purposes of the fund)	\$1,385.69
United States Defense Bonds, Series "G"	3,000.00
Total	\$4,385.69

A prize of \$100.00 was awarded for a paper entitled "Dermatotherapy as Applied to Diseases of the Eyelids" by "Eidal," pseudonym for Dr. Arthur Linksz, and also a prize of \$50.00 for a paper entitled "Prostatic Hypertrophy" by "John H. Doe," pseudonym for Dr. Rolf Lium. The accounts of the Treasurer have been examined and found correctly cast and properly vouched.

HENRY O. SMITH
SAMUEL T. LADD
FREDERIC P. LORD, Secretary

The scientific session was concluded by an address, entitled "Recent Treatment of Gonorrheal Infections in the Female," which was presented by Dr. Fred L. Adair, of Chicago.

The banquet was held at the Hotel Carpenter, with Dr. Ralph W. Tuttle as toastmaster. President-Elect Timothy F. Rock, of Nashua, and Governor Robert O. Blood spoke very briefly. Dr. Ernest E. Lyons then presented an address, entitled "The Last Illness of Sir Joshua Reynolds," and showed many lantern slides of paintings. This was followed by a talk by President Dolloff.

CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28441

PRESENTATION OF CASE

First admission. A fifty-two-year-old truck driver came to the hospital because of swelling of the abdomen.

Five years prior to admission the patient noticed that his abdomen was becoming swollen. Three years later he noticed a feeling of abdominal fullness that developed approximately twenty minutes after eating. At times, especially when constipated, this was accompanied by pain on both sides of the abdomen at about the level of the umbilicus. These symptoms were relieved by soda. At the same time he noticed the appearance of a yellowish discoloration of the skin, unaccompanied by nausea, vomiting, pain or clay colored stools. He also developed exertional dyspnea and ankle edema. One year before entry, urinary urgency, frequency, hesitancy and dribbling and nocturia developed. These symptoms became progressively worse to the day of admission. There was no loss in weight or any blood in his urine or stools. For many years he had occasionally drunk 3 or 4 ounces of whisky each day, but usually it was less; however, his diet was said to have been quite adequate.

His wife and two children were living and well. His wife had had no miscarriages.

The patient was born in Italy and came to America at the age of three. His vision had recently become poor, but there was no double vision, blurring or spots before the eyes. At the age of eighteen or nineteen, he had had gonorrhea without known sequelae. He denied a penile sore.

Physical examination revealed a heavy set man who appeared slightly dyspneic. The skin and scleras were obviously yellow. The abdomen was "massive," tense and bulging. There was a marked wasting of the soft parts of the face, arms and chest. No odor of acetamide was detected on the breath. There was a marked degree of clubbing of the fingers and toes. The chest was barrel shaped. Examination of the lungs was negative except for bilateral posterior basal rales. The heart was not enlarged. A loud systolic murmur was audible over the entire precordium but best heard in the fourth interspace to the left

of the sternum. A fluid wave was easily elicited, and there was shifting dullness. Rectal examination revealed internal and external hemorrhoids. The prostate was nodular and not tender. There was edema of both lower extremities.

The blood pressure was 144 systolic, 60 diastolic. The temperature was 98°F, the pulse 81, and the respirations 20.

Examination of the blood revealed a hematocrit of 170 per cent, a red cell count of 2,250,000, with a hemoglobin of 22 per cent, and a white cell count of 2300 with 71 per cent polymorphonuclears. In the blood smear there was extreme variation in the size and shape of the red cells. Many macrocytes were present, but the average size of the red cells was below normal; there was no polychromatophilia; the granulocytes appeared old. The urine had a specific gravity of 1.015, and the sediment contained 2 white cells, a rare red cell and occasional epithelial cells and coarse granular casts per high-power field. The blood Hinton and Wassermann tests were positive. The van den Bergh test was first reported normal; when repeated four days later it was said to have been slightly above normal with a biphasic reaction. The blood protein was 5.4 gm per 100 cc. The prothrombin time was 22 seconds (normal, 20 seconds).

Roentgenograms of the chest showed slight generalized cardiac enlargement. The aorta was not remarkable, and the lung fields were clear. An abdominal paracentesis yielded 5000 cc. of clear fluid with a specific gravity of 1.012 and a cell count of 900. The fluid did not clot on standing. The spinal fluid was essentially normal; the total protein content was 30 mg. per 100 cc, the colloidal gold curve 0012211000, and the Wassermann test negative.

After paracentesis an irregular mass was felt below the costal margin, which was believed to be the liver. On the seventh day after admission, under local anesthesia, a peritoneoscopy was performed; 6500 cc of straw colored fluid was aspirated. The liver could not be seen anywhere because thick masses of omentum were adherent to it over both lobes. On the left the omentum was also adherent to the anterior abdominal wall and was very vascular suggesting a spontaneous omentopexy. From the general point of attachment of the omentum from inspection and from percussion after removal of the fluid, it did not appear that the liver was enlarged. The lower abdomen and pelvis appeared normal. The patient received supportive and antisyphilitic therapy, including potassium iodide and bismuth subsalicylate, and was discharged moderately improved on the twelfth day.

Second admission (seven months later). Following discharge, the patient did poorly. Ascites reaccumulated rapidly, and during the month prior to admission required a tap every four to six days, when 4000 to 5000 cc. of fluid was recovered. Intermittent jaundice had been observed in the Out Patient Department. The potassium iodide and bismuth subsalicylate had been continued. The patient's appetite had been fair, although he severely limited his fluid intake. On the day of admission he developed a dull aching pain beneath the right costal margin.

Physical examination revealed a thin, emaciated dyspneic man who was obviously acutely and chronically ill. The skin was dry, yellow and sallow. There were multiple port-wine telangiectases over the hands and forearms. Expansion of the chest was limited. There were diminished to absent breath sounds over this area with decreased tactile and vocal fremitus. There was flatness to the level of the fifth interspace posteriorly and laterally. Multiple coarse rhonchi were audible in both chests. The heart was not enlarged. There was a great deal of abdominal fluid. After withdrawal of 6000 cc. of fluid the liver edge was felt four fingerbreadths below the costal margin; the edge was rough and not tender. The abdominal-wall veins were prominent. A mass could be felt in the left upper quadrant. An umbilical venous hum was audible. There was a moderate pitting edema of the legs and abdominal wall.

The blood pressure was 120 systolic, 60 diastolic. The temperature was 98°F., the pulse 82, and the respirations 20.

Examination of the blood revealed a red-cell count of 1,920,000 with a hemoglobin of 3.2 gm. and a white-cell count of 10,600 with 78 per cent polymorphonuclears. The smear resembled that of the first admission. The urine and stool examinations were negative. The blood protein was 5.6 gm. per 100 cc. An x-ray film of the chest revealed extensive increased density involving the lower two thirds of the left lung field, more marked laterally. The heart was about normal in position. Abdominal paracentesis was repeated several times, but the fluid reaccumulated rapidly. A thoracentesis yielded 1100 cc. of dark-amber, slightly cloudy fluid. This did not represent all the chest fluid, since dullness was still present to the fifth interspace.

Terminally, the patient was very uncomfortable because of dyspnea. Hoarseness developed, and the patient talked with a whisper. Examination of the larynx revealed a moderate edema of the arytenoid cartilages, which somewhat limited the excursion of the true cords; the airway was perfectly adequate. The patient became drowsy

and stuporous, and died on the sixteenth day after admission.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM B. BREED: This morning I read this case over once, and am therefore only one reading ahead of you. I shall set up the diagnosis that I have in mind, and perhaps between us we shall be able to support it—or discredit it. I will say, to begin with, that I think this man had portal cirrhosis of the liver with superimposed hematoma. Now let us read the material presented. Please give as much thought as you can to it with that diagnosis in view, and if you do not like the way things are going, please interrupt at any time.

* * *

Now that we have read the story again, I wonder if anyone is interested in the original diagnosis that I set up. (No answer.) Is anyone disinterested? (Silence.) This is an open forum; everyone's opinion has equal standing.

First of all, let us see if we can account for everything on the basis of syphilis, which has to be considered in view of the positive Hinton test. He obviously had liver disease. I do not know very much about diffuse syphilis of the liver. It is quite uncommon. Gummatous involvement of the liver is the commonest form of liver disease in syphilis, but such a manifestation should respond to iodides and bismuth, which apparently this did not. I see no other evidence anywhere of syphilis, such as aortitis, aneurysm or nervous-system involvement, and so I am willing to ignore the positive Hinton test as being the only indication of syphilitic infection and, therefore, not important as a cause of this man's illness and death.

Did he have metastatic cancer? That is the other most obvious alternative. As to cancer of the prostate, I noticed that the prostate was nodular but not tender. It does not say how hard it was. How long ago was this man in the hospital?

DR. TRACY B. MALLORY: About a year and a half ago.

DR. BREED: Even a year ago it is probable that if they thought that the patient had cancer of the prostate with metastases they would have castrated him. Cancer of the prostate, moreover, does not as a rule metastasize to the liver. It may do so but the metastases are usually in the bones, in the lungs and in the brain. Is that not correct, Dr. Mallory?

DR. MALLORY: The bones above all.

DR. BREED: Thank you. We have no evidence here to make a diagnosis of cancer of the prostate. He had urgency and frequency at one time, but we do not know whether it persisted. There

was no obstruction to the urinary output. I am not willing to make a diagnosis of cancer on the lone statement that he had a nodular prostate.

We have enough here to make a diagnosis of portal cirrhosis. He had ascites and a history of alcohol, even though his diet was said to have been adequate. It is too bad that we have no

extremely low figure. Toward the end the patient accumulated fluid in his left pleural cavity. That is perfectly all right in the presence of cancer in the liver even though the fluid was not on the right side—the more usual site.

There are still some findings that I cannot adequately explain. The question is, Are most of



FIGURE 1

x-ray films of the esophagus or some liver-function test. I am surprised that they were not done, because I suspect that he was discharged the first time with diagnoses of portal cirrhosis and syphilis. It seems to me that they should have tried a little harder to confirm the former.

What about the clubbing of the fingers? That is a hard one. I am going to say that it was congenital clubbing of the fingers. He had nothing on physical examination or by x-ray study to indicate a systemic cause of clubbing of the fingers, except possibly a congenital heart lesion. We know he had some enlargement and a loud systolic murmur on the left side of the sternum. He may have had a congenital lesion, but I doubt it. There were no other manifestations, such as cyanosis and typical murmurs. The reason I suspect he had cancer of the liver is the extreme degree of anemia and the rapid downhill course once he became sick. Apparently for five years he had had some fullness in the abdomen, which I explain on the basis of early portal cirrhosis, and during the last year of his disease he went downhill rapidly and developed a severe degree of anenia. The low white-cell count in the beginning is consistent with liver disease. The serum protein, if accurate, was depressed, but not to an

the things that appear here consistent with one diagnosis? Assume, for the moment, that we have ruled out syphilis and metastatic cancer from either the prostate or gastrointestinal tract, which by the way was not examined. That leaves us with malignant disease in the liver superimposed on what appears to be portal cirrhosis, and congenital clubbing of the fingers.

The peritoneoscopy does not help us at all, except to show that there had been adhesions and that the omentum had been pushed up against the liver to create a spontaneous omentopexy. I am going to assume that the mass in the left upper quadrant felt after paracentesis was an enlarged spleen. That is the commonest mass felt in the left upper quadrant. The hoarseness without obvious signs of paralysis does not interest me very much. There was no evidence of pressure on the trachea. There was only moderate edema of the arytenoid cartilages, and no paralysis of the cords. Aside from syphilis and metastatic cancer, what else may he have had? Has anyone here, having read this over with me, other suggestions as to the cause of this man's illness and death? (No answer.) Then I take it we all agree that I have mentioned at least three of the most likely diagnoses.

DR. RICHARD H. SWEET: Why is it necessary to assume that the patient had a primary cancer of the liver or hepatoma? Why does not cirrhosis account for the whole picture?

DR. BREED: I say that because he went downhill so rapidly, with such a severe degree of anemia and fluid in the chest.

DR. SWEET: That is inconsistent with cirrhosis alone?

DR. BREED: I believe so.

DR. ALLEN G. BRAILEY: The history covers a period of five years!

DR. BREED: We do not know how much anemia the patient had until seven months prior to death, when the anemia was discovered. How do you know he had anemia for a longer period of time? It says that for five years he had had swelling, that for two years there had been fullness and that for only a year previous to admission he had had these new symptoms. For a year and a half he was incapacitated, and in seven months he was dead.

DR. REED HARWOOD: I am not impressed with the rapidity of the patient's down-hill course. He had severe anemia—a red-cell count of 2,000,000—seven months before he died. Seven months is a long period to live with an anemia of that severity due to cancer, is it not?

DR. MALLORY: There is one thing that is not clearly brought out in the summary. He had an enlarged spleen, but several examiners thought that they could feel another epigastric mass, which seemed to be attached in some way to the liver.

DR. BREED: We know by peritoneoscopy that he had a mass of omentum stuck up against the liver. Do you think one could have felt this mass of omentum through the abdominal wall, Dr. Sweet?

DR. SWEET: I doubt if one could unless there was something in it.

DR. BREED: Why, in all this time, if they felt an epigastric mass and suspected cancer or a lesion in the gastrointestinal tract, did they not investigate it? They could not have thought much of it because they sent him home with no diagnosis so far as the gastrointestinal tract was concerned. If they did that, how can I be expected to add to the diagnosis now? I also wonder a little bit why they did not think enough of the diagnosis of portal cirrhosis to go farther with it. Did they?

DR. BENJAMIN CASTLEMAN: Do you think that they may have made a diagnosis of syphilis on the first admission and sent him home on anti-syphilitic treatment to see what would happen?

DR. BREED: That seems obvious. They sent the patient home under treatment with a diagnosis of syphilis. He did not do well and re-

turned. Nothing further was done to establish a diagnosis. I still think that they should not have been quite so certain that this was syphilis, even though he had a positive Hinton test. I do not believe the diagnosis was accurate enough.

DR. MALLORY: Assuming that the history is correct and that he took never more than 3 or 4 ounces of whisky a day and usually less, do you still maintain that your diagnosis of portal cirrhosis is correct?

DR. BREED: I do not quite get the import of that question.

DR. MALLORY: I am asking a personal question, Dr. Breed. If the history of alcoholic intake is correct, do you want the patient to be proved to have portal cirrhosis?

DR. BREED: From a personal point of view? No. Seriously, however, I question the adequacy of his diet.

Have you any other suggestions that might set me right? I can see that the wind is blowing the wrong way. Is not someone here brave enough to come forward and help out Dr. Mallory? He has something on his mind. It is not because you do not want to speak up but because you do not know, is that right? (No answer.) Then I shall have to leave it that way.

CLINICAL DIAGNOSES

Portal cirrhosis.
Banti's syndrome.
Syphilitic cirrhosis?
Asymptomatic syphilis.

DR. BREED'S DIAGNOSES

Portal cirrhosis.
Hepatoma.
Latent syphilis (serologic).

ANATOMICAL DIAGNOSES

Syphilitic cirrhosis of liver (hepar lobatum).
Icterus.
Splenomegaly.
Ascites.
Hydrothorax, left.
Pulmonary atelectasis, left lower lobe.
Osteoarthropathy: fingers and toes.
Pulmonary tuberculosis, healed: apical, bilateral.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Some years ago, I looked up all the cases of syphilis of the liver that had come to autopsy, and out of 20 cases, 18 were accidental findings at autopsy without referable symptoms in the clinical history. Two had symptoms; but in one of these there was amyloid disease, which may well have been responsible for the ascites, so that

left only 1 out of 20 patients who did have symptoms.

Syphilis of the liver is what this man had. The liver was considerably smaller than normal. It presented marked deep fissures dividing it into eight or ten lobes instead of the normal five (Fig 1). You will note there is an almost pedunculated mass that dangles from the hypertrophied left lobe; this probably was at some time felt as the epigastric tumor. The shrunken right lobe is completely wrapped in omentum. When nodules are actually felt on a liver, it always means either tumor or syphilis of the liver. In a patient with symptoms of cirrhosis of five years' duration the recognition of palpable nodules on the lower margin of the liver would have led me to make the same diagnosis as Dr. Breed did; it seems the most reasonable one. I should hardly have expected a liver of this sort to have produced the characteristic symptoms of cirrhosis lasting over a period of five years.

I think the reason this patient made no improvement on syphilitic therapy is that the active stage of gumma formation was past history, when they started treating him he already had a scarred liver and one could hope to accomplish nothing with treatment.

There is no explanation of the marked hydrothorax on the left except the presence of ascitic fluid. Whenever there is ascitic fluid, it never surprises me to see a pleural effusion develop, although it is more apt to appear on the right than on the left; but it can develop on either side, as in the cases of ovarian fibroma that Dr. Joe V. Meigs has called to our attention.

We found no other evidence of syphilis. He had a normal cardiovascular system. He did not have anything wrong with the urinary tract.

DR. BREED: Was the clubbing of the fingers and toes congenital?

DR. MALLORY: I do not believe so. It was probably due to cirrhosis. A significant number of cases of cirrhosis of the liver have clubbing of the fingers.

A PHYSICIAN: What about the prostate?

DR. MALLORY: It was normal.

CASE 28442

PRESENTATION OF CASE

A forty-seven year old man was admitted because of severe abdominal pain.

The patient was known to have had a high blood pressure for many years but had been quite well until one month before entry. At this time he had an attack of moderately severe substernal

pain, which lasted two days and then cleared completely. During the succeeding month he was well and active. Several hours prior to admission he developed an excruciating pain centered in the lower abdomen. At times he believed the pain radiated into the legs. There was no radiation of this discomfort to the chest. He vomited once. The patient collapsed soon after the onset of the pain and was immediately brought to the hospital. After reaching the hospital he noticed numbness of the right arm.

Physical examination revealed a semicomatose, thickset man lying quietly in bed complaining of severe lower abdominal pain. There was no cyanosis or dyspnea, and the neck veins were not distended. The examination of the lungs was negative. The apex impulse of the heart was felt in the fifth interspace, 11 cm. to the left of the midsternal line, which was 3 cm. beyond the midclavicular line. A rather harsh, moderately strong, systolic murmur was audible at the base of the heart in the aortic area and was transmitted to the neck, to the left of the sternum, and to the apex. A loud blowing diastolic murmur was heard in the aortic area, but was transmitted to the cardiac apex. The aortic and pulmonic second sounds were equal in intensity. The abdomen was soft and slightly protuberant, with rather generalized tenderness in the upper portion. A systolic murmur was prominent in the epigastrium; the peristaltic sounds were normal. The right arm was pulseless and slightly cooler than the left.

The blood pressure was 205 systolic, 95 diastolic, in the left arm; it could not be obtained in the right arm. The blood pressure was 220 systolic, 95 diastolic, in both legs. The pulse in the left arm was regular and of good quality, with a rate of 60. The temperature was 97.8°F.

An electrocardiogram showed a normal sinus rhythm with a rate of 50. T₁ was low and diphasic. The T waves were very low in Leads 2 and 4, and T₃ was high. P₁ was diphasic. There was a considerable amount of left axis deviation.

Several hours after admission the patient said he felt better and indicated that the right arm was less numb and his feet less cold. The right hand and arm remained cool, but there was a weak but definite radial pulse. Four and a half hours later, less than twelve hours after reaching the hospital, the patient expired quietly within two or three minutes.

DIFFERENTIAL DIAGNOSIS

DR. REED HARWOOD: After reading the first two sentences I think we should consider the

possibility that this man had had a myocardial infarction. We might think then, if it were not for the numbness in his arm, that this episode of excruciating abdominal pain was the result of the separation of an embolus from a mural thrombus, which lodged in the bifurcation of the aorta. It is unusual for a man who has had severe pain to become semicomatose so suddenly. The fact that he had no cyanosis, dyspnea or signs in his lungs shows that he was not in congestive failure. The position of his heart suggests an enlarged left ventricle or possibly that the heart had been pushed to the left.

He might have had a systolic murmur for many years. He had had hypertension for a long time, and he might have had previous disease of the aortic valve. Probably he did not have the loud blowing diastolic murmur before the onset of his present illness. I say this because he was known to have had hypertension for a long time, and I should think that the doctor would have detected a loud blowing diastolic murmur. I think we can reason therefore that he did not have the diastolic murmur for more than a few hours. He probably did not have the systolic one for much longer either; otherwise, I think it would have been mentioned in the record.

Let us consider then the possible causes of a diastolic murmur in the aortic area. The first that comes to mind is syphilitic aortitis. He would have had a murmur of aortic regurgitation for a long time if he had had syphilitic aortitis. The same is true if he had had rheumatic heart disease with aortic regurgitation. I am going to exclude these two diagnoses on the basis that I believe that this murmur was of very short duration. Another possibility to be mentioned only to exclude it is rupture of the aortic cusp. I know very little about this condition, but I do not believe it would produce the numbness in the right arm and so forth. Although he had signs of aortic regurgitation, there is one very interesting finding—namely, the aortic and pulmonary second sounds were equal in intensity. I am going back to that and explain the probable mechanism when I have made my diagnosis.

The fact that the blood pressure in the legs was essentially the same as in the left arm rules out fairly well the possibility of a rider embolus.

I think we can interpret the electrocardiogram as follows: the interpreter was trying to find something abnormal, but he had to admit in the end that the patient did not have anything suggesting coronary thrombosis or myocardial infarction. It did suggest, however, that the patient had left ventricular hypertrophy, as shown by the axis deviation. This is consistent with the story of long-continued hypertension. The electrocardio-

gram, to my way of thinking, rules out quite well the possibility of myocardial infarction two months ago, and we can dismiss that diagnosis here and now.

In summary, the patient had severe pain in the abdomen, numbness and lack of pulse in the right arm and died suddenly. I can think of only one diagnosis that will fit the findings in this case and that is dissecting aneurysm. We might argue that the age, forty-seven, was rather young for that condition. However, I have seen cases reported considerably younger. So I do not believe we need to rule out the possibility of dissecting aneurysm on that single finding. Then there is the question of whether he had syphilis as a basis for his aneurysm. Dissecting aneurysm can occur in patients with syphilis in the aorta and cases have been reported. The late Dr. Soma Weiss, however, believed that if dissecting aneurysm did occur in a case of syphilitic aortitis it was coincidental rather than a result of the syphilitic process. In fact there is some suggestion that the inflammatory process of syphilis may protect the patient against this accident. I am going to say that he probably did not have it.

There is another interesting point that I want to discuss—that is, the matter of his being semicomatose. Patients with severe, sudden onset of pain in the abdomen and chest do not become comatose suddenly unless they have a sudden lowering of the blood pressure that is sufficient to produce cerebral anemia. We know that this patient did not have sudden lowering of the blood pressure, but may he not have had an anemia, at least of one cerebral hemisphere? We notice he was pulseless in the right arm. If he had a dissecting aneurysm, this means that the dissection must have involved the right innominate artery. In keeping with this is the fact that at the time when a weak but definite pulse could be found, he was not semicomatose and was able to say he felt better. Then, while he seemed to be improving, he suddenly died.

Dissecting aneurysms very frequently rupture somewhere along their course, and I think the most frequent location of rupture is into the mediastinum or into the pericardium. Either of these is rapidly fatal, and I do not see how we can distinguish between them. It is possible also that the aneurysm could have ruptured into the abdominal cavity, but in that case I do not believe he would have died so suddenly. So I am going to say that he had dissecting aneurysm of the aorta originating probably in the arch or in the descending portion of the arch, which dissected its way to the aortic ring and down through the abdomen and stopped somewhere in the region

of the bifurcation. He also probably had left ventricular hypertrophy.

I said that I was going to explain why he had the loud blowing diastolic murmur and still had an audible aortic second sound. Perhaps I should have said that I was going to try to explain it. I believe that the aneurysm distorted the aortic ring in such a way that a diastolic murmur was produced. Although the cusps clicked shut momentarily, it is probable that some blood did leak back into the heart.

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Dissecting aneurysm of aorta.

DR. HARWOOD'S DIAGNOSIS

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Dissecting aneurysm of aorta, with perforation into the pericardium.

Hemopericardium.

Media necrosis cystica aortica.

Nephrosclerosis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The same diagnosis as Dr. Harwood's was reached on the ward and was substantiated at autopsy. There was an extensive dissecting aneurysm with a tear in the intima of the aorta about 3 cm. above the aortic valve. It dissected back as far as the annulus, partially surrounded the mouths of the coronary arteries but did not occlude them. It also dissected forward over the arch for a short distance into the innominate and left carotid arteries and 3 cm. down the left subclavian artery. In the subclavian, it had failed to rupture back through the intima so the subclavian was completely blocked by a projecting knuckle of intima. Dissection continued down the thoracic abdominal aorta into both iliac vessels, but in each of these rerupture of the intimal layer had occurred, so that the circulation was quickly re-established in both legs, if it was ever completely interrupted. There was a dissection for 1 cm. along the superior mesenteric artery,

but again there was either no interference with the blood supply to the bowel or only a transitory one, because there was no discoloration of the intestines.

We found nothing to suggest that the aortic valve was not functioning perfectly well, and I have no clear explanation of the diastolic murmur. One is heard, however, every once in a while in these cases of dissecting aneurysm. It is at least possible that the jagged, rough tear in the intima creates a V-like flap between one column of blood in the old lumen of the aorta and the other column in the newly formed vessel outside. One can imagine it flapping back and forth to make an odd variety of murmurs, perhaps in both systole and diastole. The immediate mechanism of death, as Dr. Harwood prophesized, was rupture into the pericardium, with cardiac tamponade. The kidneys showed moderately severe nephrosclerosis.

DR. ALLEN G. BRAILEY: What do you think of the coma? It was not shock?

DR. MALLORY: It is hard to see how it could have been shock when the systolic blood pressure was 220. I should think that the carotid artery may have been temporarily obstructed by external pressure. There was no extensive dissection along the carotid.

The aorta in this case showed a very good example of so-called "media necrosis cystica," which is often to be found in cases of dissecting aneurysm. It is a condition that occurs only in elastic arteries, and the dissection is ordinarily limited to arteries that have this elastic structure. For that reason, dissection extends only a very short distance along most of the branches of the aorta, such as the coronary and renal vessels, which are muscular arteries, but may extend several centimeters along the subclavian and iliac vessels, which have a structure similar to that of the aorta.

DR. BRAILEY: Is this always associated with high blood pressure?

DR. MALLORY: I cannot answer that accurately.

DR. HOLMES: There was no evidence of syphilis?

DR. MALLORY: No; in a dissecting aneurysm, there almost never is.

perience in medical defense. Dr. Arthur W. Allen, chairman of the Committee on Medical Defense of the Massachusetts Medical Society, states that the record

the facts presented, each member may better select that insurance company which meets his individual needs best. Reliability is paramount, experience in the field is of con-

TABLE 1. Comparative Rates for Malpractice Insurance.

COMPANY	GENERAL PRACTICE (NO SURGERY)		GENERAL PRACTICE SURGERY AND DIAG. X-RAY		GENERAL PRACTICE AND THERAP. X-RAY	SPECIALISTS IN X-RAY	SPECIALISTS IN SURGERY, OBSTETRICS AND ORTHOPEDICS	SPECIALISTS IN E, E, N. AND T.
	\$5- 10,000	\$10- 30,000	\$5- 10,000	\$10- 30,000				
Medical Protective Company ..	\$24.00	—	\$32.00	—	—	—	—	—
United States Fidelity and Guaranty Company .	—	\$20.00	—	\$40.00	\$60.00	\$70.00	\$60.00	\$40.00
American Motorists Company	\$20.00*	\$26.00*	\$20.00*	\$26.00*	—	—	—	—
Metropolitan Casualty Company .	—	\$20.00	—	\$40.00	\$60.00	\$70.00	\$60.00	\$40.00

*Less 20 per cent, if earned

of this company in this state is good. As has been mentioned, their suit experience in Essex County is very high.

The *United States Fidelity and Guaranty Company* (assets, \$30,000,000) has not had a high suit rate in Essex County. They retain the law firm of Powers and Hall, in Boston, who have had a wide experience in defending malpractice suits. In their policy they have a dissolve attachment bond feature. Dr. Allen says that their record in this work is good. This company advises minimum limits of \$10,000-\$30,000, and believes so strongly that these limits are necessary that it does not write for less. On the other hand, the Medical Protective Company believes that \$5000-\$15,000 limits are sufficient, and will not write for more in Essex County.

The *American Motorists Company* (assets, \$10,000,000), a subsidiary of the Lumbermens Mutual Insurance Company (assets, \$41,000,000), is relatively new in the medical-defense field, although they have been in Massachusetts for ten years and now collect \$13,000 in premiums for this type of insurance. They advise \$10,000-\$30,000 limits, but will write for less.

The *Metropolitan Casualty Company* (assets, \$11,000,000) has been official for the Massachusetts Dental Society for nearly twenty-five years. A prominent feature of their policy provides payment of premium on appeal bonds without limit. This company pays \$15 a day for not more than seven days to the defendant doctor for loss of time while in court.

While this study was in progress, and after one set of rates had been offered, Ladd and Milne, in Haverhill, obtained the following concession from the American Motorists Insurance Company, which they represent: for all physicians in Essex County, whether engaged in general practice, major surgery or another specialty, but excluding those physicians using x-ray and radium for therapeutic purposes, the premium of \$20.00 for \$5000-\$15,000 limits is offered; for \$10,000-\$15,000 limits, \$24.00; and for \$10,000-\$30,000 limits, \$26.00. The company states that if a substantial amount of the business in this county is obtained over a period of one year, the rate will continue. No assessment can be made against the policyholder, and a dividend of 20 per cent, if earned, is returned to him. It is a legal reserve stock company, but is owned and operated by the Lumbermens Mutual Insurance Company. According to Ladd and Milne, the company offers this rate schedule only through their agency.

In summary, this committee chooses to recommend no one company for all the members. It is hoped that from

siderable importance, and a reasonable rate is desired. The committee will gladly assist any member by allowing him to examine any of the data and all the letters that we have collected as a result of this investigation.

GUY L. RICHARDSON, M.D., *Chairman*
GEORGE J. CONNOR, MD
ALDEN B. GEORGE, MD.

NEW HAMPSHIRE MEDICAL SOCIETY DEATHS

COTTON — CURTIS B. COTTON, M.D., of Wolfeboro, died August 6. He was in his seventy-eighth year.

Dr. Cotton, the son of Joel F. and Elivna (Gilman) Cotton, was born in Moultonboro and graduated from the University of Vermont College of Medicine in 1888. He was a member of the New Hampshire Medical Society and the American Medical Association.

He is survived by his widow, a son and a sister.

ROWE — ARTHUR J. ROWE, M.D., of Penacook, died September 9. He was in his seventy-fifth year.

Born in South Barnstead, the son of Dr. James W. and Emma (Clark) Rowe, Dr. Rowe received his degree from Dartmouth Medical School in 1899. He was a member of the New Hampshire Medical Society and the American Medical Association.

He is survived by his widow, Mrs. Ida (Avery) Rowe, three brothers and a sister.

WAR ACTIVITIES PROCUREMENT AND ASSIGNMENT SERVICE

The following release was recently received from the Washington office of the Procurement and Assignment Service:

The Directing Board of the Procurement and Assignment Service is pleased to announce that 95 per cent of the 1942 procurement objective of medical officers for the armed forces has already been met. Toward this total a number of states have supplied more than their share of physicians. Only a few states are lagging behind in their quotas, and it is from these states that the additional physicians needed during the current year should come.

The recruitment of such a large number of physicians in a few months is a remarkable achievement and another demonstration of the traditional patriotism and unselfishness of the medical profession. In this achieve-

of the bifurcation. He also probably had left ventricular hypertrophy.

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THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

NAVAL MEDICAL OFFICER PROCUREMENT

Attention is called to a letter from the Office of Naval Officer Procurement, published elsewhere in this issue of the *Journal*, which emphasizes the need for obtaining medical officers from Massachusetts. Apparently, physicians who have previously been rejected because of minor physical defects may now receive favorable consideration.

MASSACHUSETTS LABORATORY TECHNOLOGISTS RESERVE CORPS

A LETTER in this issue of the *Journal* calls attention to an extremely necessary addition to the activities of the Massachusetts Committee on Pub-

lic Safety. Because of an acute shortage of adequately trained laboratory technologists, many hospitals in the Commonwealth lack the specialized services that would be required in the event of wholesale bombing or other civil disasters. To correct this situation, the Committee on Public Safety is organizing the Massachusetts Laboratory Technologists Reserve Corps. By this means, each of the one hundred and twenty-four emergency (casualty receiving) hospitals in Massachusetts will be assigned technicians up to its needs, sometimes as many as three or four, for specialized work in an emergency.

The corps, which will consist of women trained as hospital technologists, will be organized in a manner similar to that of a military group. The members are expected to number approximately three hundred and fifty. The personnel will include both experienced technologists not at present engaged in such work and those who are already employed. Under the direction of nine regional directors, the corps will function in all parts of the Commonwealth.

The Massachusetts Committee on Public Safety is to be congratulated for its zeal in preparing the Commonwealth against possible disaster. The formation of this corps is a vital contribution to civilian defense.

THE SENESCENT SKIN

Now that the older age groups constitute a large proportion of the population, more interest has been aroused in geriatrics, but as yet, few phases of this branch of medicine have been explored to any extent. Even the most accessible organ—the skin—has been given little study.

In this issue of the *Journal*, attention is called to the many varied conditions that contribute to generalized itching in old persons. Not only local causes but also general factors, both external and internal, act to produce this symptom, which can have a very serious effect on the patient: general pruritus may be an early manifestation of a serious disease, when, by interfering greatly with sleep

and nutrition, it may thus act to lower further the resistance of a patient already combating the inroads of a disease of other organs. In general, eczema, keratoses of various types, pruritus and cancer are the commonest diseases of the skin of old persons. At the same time, it should not be forgotten that other skin diseases—those of childhood and of middle life—may be found in people of this age group and that the diagnosis may be missed by reason of failure to consider such possibilities.

Grossly, as the years pass, the skin becomes dry, thinner, less elastic and wrinkled. Pigmented areas, dilated vessels and small scaly areas may develop. Histologically, according to Hill and Montgomery,* the greatest changes occur in the collagen and elastic tissue, with some atrophy of the rete pegs. Investigation concerning the physiologic and chemical changes in the skin of this older group has received but slight attention. In addition, there is little knowledge of the effect on the skin of senile circulatory changes—the failing heart muscle, the fibrotic changes in arterics and the loss of elasticity of the veins and capillaries. Such changes cannot fail to have some relation to morbid processes in the skin. Whether the reduction in glandular activity and the subsequent dryness are results of circulatory change is not known. The effect of the aging process elsewhere or of pathologic processes in other organs is obscure. Much remains to be learned of the part played by the nervous system, by hormones and vitamins and by nutrition in aging of the skin. Truly, a large realm of investigation lies open to the explorer in this field.

*Hill, W. R., and Montgomery, H. Regional changes and changes caused by age in normal skin: histologic study. *J. Invest. Dermat.* 3:231-245, 1940.

MEDICAL EPONYM

SCANZONI MANEUVER

The description of this maneuver appears in "Die geburtschilflichen Operationen [Obstetric Operations]," which was issued by its author, Professor Friedrich Wilhelm von Lichtenfels Scanzoni (1821-1891), of Würzburg, in the form of a reprint, with revisions, of a portion of the third volume of his *Lehrbuch der Geburtshilfe* [Text-

book of Obstetrics] (1852). A portion of the translation follows:

Our procedure under these circumstances is as follows: If the head lies with the brow anterior and turned to the left, so that the longitudinal suture runs in the right diagonal diameter, the left blade is applied in front of the left sacroiliac synchondrosis, the right behind the right oval window [*cirunder Loche*]. . . . The head is then rotated, by turning the instrument from right to left through one eighth of a circle, so that the longitudinal suture lies parallel with the transverse diameter of the pelvis.

Both blades of the forceps are now removed and re-applied so that the left blade lies behind the left oval window, the right in front of the right sacroiliac joint, whereby the occiput may be drawn under the pubic arch by again rotating the instrument.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

HEART DISEASE

In the tabulation that appeared in the first installment of the maternal-mortality study for 1941, the deaths of 42 women were attributed to medical causes. These can be broken down into the following groups:

Heart disease	22
Pneumonia	12
Hypertensive nephritis	2
Meningitis	2
Gastric ulcer	2
Tuberculosis	1
Colitis	1
Total	42

Of the 22 deaths that occurred as a result of heart disease, in 8 the patient was undelivered, 8 followed normal delivery, 5 followed operative delivery and 1 was associated with miscarriage. Autopsy was performed in only 1 case.

The undelivered cases emphasize the seriousness of heart disease during pregnancy and prove beyond question that heart disease during pregnancy alone may cause death. From this standpoint, the deaths are, of course, preventable, and the medical profession is responsible for them if its advice was sought and abortion not advised. If these patients had been told to avoid pregnancy and if they had followed this advice, the deaths would not have occurred. Religious beliefs, however, on the part of the physician or the patient may well have played a part in these fatalities.

The cases of the 8 patients who died undelivered are reviewed briefly.

The first was a patient who, at three months, developed symptoms of heart failure; she was admitted to the hospital two months later with cardiac decompensation and died undelivered, in spite of treatment. Although no autopsy was performed, this patient was known to have had rheumatic heart disease and should have been warned against becoming pregnant; and, in the event that pregnancy did take place, abortion should have been performed in the early stage.

The second case was that of a patient who had had two previous pregnancies and who was known to have a definite heart lesion; in her third pregnancy she had attacks of tachycardia and palpitation. When seven months pregnant she became acutely decompensated, entered the hospital and died a few hours later. The criticism of the first case can be reiterated here.

The third patient, who had a history of a cardiac lesion since childhood, was a primipara; she was being prepared for a cesarean section when she had acute cardiac failure and died fifteen minutes later. There is little to be said in criticism of this case.

The fourth patient was known to have had rheumatic heart disease with a double mitral lesion for years. She was seen at first by her physician when about five months pregnant, at which time she was in cardiac distress, but refused hospitalization. When seen a week later at home, she was in extremis and died shortly. This fatality can be attributed either to the patient's ignorance in not having sought medical advice earlier in pregnancy or to religious dogma. She should never have become pregnant.

The fifth case in this group was a patient who, with a history of rheumatic heart disease since childhood, was seen first at three months and again at six months, when, because of signs of decompensation, she was sent to the hospital. Her stay there lasted only six days. She should not, of course, have been allowed to go home, but she was said to have been unco-operative. When she was approximately at term, acute cardiac decompensation developed and she died undelivered. The treatment of this case was obviously unintelligent.

The sixth patient, a multipara with rheumatic heart disease, did not consult a physician until near term, at which time she had an attack of acute cardiac failure and was practically moribund at the time of her arrival. This patient was not in labor and died undelivered en route to the hospital.

In the two other cases in this group, the records are not adequate. One patient is known to have had rheumatic heart disease of long standing; she died undelivered at six months. The other had the same history of rheumatic heart disease and died near term.

The following are the records of the 8 patients who died of heart disease following normal delivery. The first was a patient who, at six months, was hospitalized and given digitalis for cardiac decompensation and who was sent home six weeks later. She re-entered the hospital at approximately eight months, being in poor condition and in mild labor. A living 4½-pound baby was delivered, but the mother went steadily downhill and died on the fifth post-partum day.

The second patient was delivered normally but developed cardiac insufficiency seven weeks post partum; in spite of treatment, she died five days after the onset of the attack.

The third patient, a multipara who gave a history of rheumatic heart disease, entered the hospital at about eight months with cardiac decompensation associated with psychosis. She delivered herself spontaneously at term; but marked decompensation immediately followed delivery, and she lived only forty-eight hours.

The fourth patient delivered herself at term after a very short labor. Since she had rheumatic heart disease, she had been warned against pregnancy; she was hospitalized at seven months because of decompensation; she improved and remained in the hospital until she went into labor at term. Following a normal delivery, she again became decompensated and died two weeks later.

The fifth case was that of a primipara with a history of rheumatic heart disease who developed definite signs of bacterial endocarditis after a short, normal labor, from which death resulted four weeks later.

The sixth patient was a multipara who had known cardiac disease associated, during her last pregnancy, with an elevated blood pressure. Labor was induced at term by rupturing the membranes, a living 9½-pound child being delivered seven hours later. Death occurred four hours after this, following the appearance of pulmonary edema.

The last two cases, whose histories are not complete, concerned patients who had long-standing rheumatic heart disease; one developed subacute bacterial endocarditis after a spontaneous delivery, and the other, having received no medical attention whatsoever during her pregnancy, succumbed from cardiac failure several hours after delivery.

Of the 5 cases of operative delivery, the first patient was delivered prematurely at seven months. At six months she developed subacute bacterial endocarditis, proved by blood culture to be due to *Streptococcus viridans*, for which she was given sulfathiazole. She started in labor at seven months and was delivered by low forceps. Death occurred a month later. There is little to be said in criticism of the handling of this case. The patient's history shows that she had had chronic endocarditis, upon which the subacute bacterial endocarditis developed.

The second patient, delivered by low forceps, was one who had rheumatic heart disease of long standing and developed arterial emboli, proved by autopsy, on the ninth post-partum day. She died thirty-four days after delivery.

The third case in this group was a patient with congenital heart disease on whom a planned cesarean section was done. Although this patient had adequate prenatal care, she did not survive the operation (which was done under local anesthesia), death occurring three days later. At the beginning of this pregnancy, the question of whether or not she should be aborted was raised, but after consultation it was decided that the cardiac condition was compatible with a safe pregnancy.

The fourth patient had rheumatic heart disease and died shortly after delivery of cardiac decompensation, and the fifth patient, whose history is inadequate, died in heart block during a low forceps delivery.

The miscarriage in this series occurred spontaneously at two months in a patient who had rheumatic heart disease, death due to congestive heart failure occurred two weeks later. Nature did the best she could for this patient.

These 22 fatal cases of known heart disease complicating pregnancy represent a little more than 9 per cent of the total maternal deaths occurring during 1941. They show how serious heart disease is in pregnancy. They emphasize the importance of adequate prenatal care, which many of these patients did not have. They bring up the questions of abortion, of sterilization and of intelligent contraceptive advice. All these problems must be met if the maternal mortality from this particular complication is to be lowered in Massachusetts.

ESSEX NORTH DISTRICT MEDICAL SOCIETY

REPORT OF SPECIAL COMMITTEE ON MALPRACTICE INSURANCE

Investigation of malpractice insurance in Essex County was prompted mainly because of the statement by one

insurance company official that Essex County was a hotbed for malpractice suits. Two other reasons that led to this study were as follows: first, refusal of one company—the Medical Protective Company, Fort Wayne, Indiana—to write for amounts greater than \$5000–\$15000 limits, although this same company admitted writing higher limits outside of Essex County, and, second, the matter of premium rates—considerably higher than in former years and not the same in all companies.

We wrote to the medical societies of several nearby states to ascertain their experience with this type of insurance.

The Connecticut State Medical Society has a group-plan policy with the Aetna Life Insurance Company. Their experience with this group plan has been highly satisfactory. The limits are \$10,000–\$25,000. The rate for minimum coverage—no surgery—is \$12.50. The rate for unrestricted practice is \$16.50.

The Medical Society of the State of New York also has a group plan, with the Yorkshire Indemnity Company. Fifty to sixty per cent of the members of the society are insured under this plan. The rate is \$8.00 for \$5000–\$15000 limits, and \$36.40 for \$10,000–\$30,000 limits. These rates include all types of practice except a ray for therapeutic purposes. The Yorkshire Indemnity Company has an agreement with the society whereby a committee from the society may inspect all the books and records of the company whenever desired. As a result of three years' experience, it was found possible to reduce the base rate \$2.00. The premium rate for x-ray therapy was dropped to \$58.00 from \$70.00—quite a difference. Complete understanding and co-operation between the society and the Yorkshire Indemnity Company make immediate rate reduction possible whenever the figures warrant it.

The Rhode Island Medical Society has a group policy with the United States Fidelity and Guaranty Company, paying \$20.00 for \$5000–\$15000 limits. Practice in medicine and surgery is unlimited.

In October, 1941, to get a cross section of the amount of malpractice business each company was writing in one city, we made a survey of Haverhill, and found as follows: American Motorists Company, 7 policies in force; Medical Protective Company, 12 policies; and United States Fidelity and Guaranty Company, 22 policies. Four physicians were found to carry no malpractice insurance.

The Aetna Insurance Company retired from the malpractice field in Massachusetts in 1920 because of poor experience.

The Medical Protective Company, which has probably had the largest share of this type of business in Essex County for the last several years, found that in one recent year more than 30 per cent of the claims pending in Massachusetts were against physicians in Essex County. The last check made by them showed a reduction of this figure to 20 per cent. They give us satisfactory explanation of this preponderance of claims in Essex County except to say that the people of this county are more suit-minded.

As to reliability, record and other pertinent factors, the four companies mentioned above line up somewhat as follows in the opinion of the committee (the comparative rates are listed in Table I).

The Medical Protective Company is relatively small as regards its capital (assets, \$2,883,700). However, they are specialists in the medical defense field, doing no other kind of business. In Boston they have an attorney—Mr. Charles Dunn, who has had much ex-

perience in medical defense. Dr. Arthur W. Allen, chairman of the Committee on Medical Defense of the Massachusetts Medical Society, states that the record

the facts presented, each member may better select that insurance company which meets his individual needs best. Reliability is paramount, experience in the field is of con-

TABLE I. Comparative Rates for Malpractice Insurance.

COMPANY	GENERAL PRACTICE (No SURGERY)		GENERAL PRACTICE SURGERY AND DIAG. X-RAY		GENERAL PRACTICE AND THERAP. X-RAY	SPECIALISTS IN X-RAY	SPECIALISTS IN SURGERY, OBSTETRICS AND ORTHOPEDICS	SPECIALISTS IN E., E., N. AND T.
	\$5- 10,000	\$10- 30,000	\$5- 10,000	\$10- 30,000				
Medical Protective Company	\$24.00	—	\$32.00	—	—	—	—	—
United States Fidelity and Guaranty Company.	—	\$20.00	—	\$40.00	\$60.00	\$70.00	\$60.00	\$40.00
American Motorists Company.	\$20.00*	\$26.00*	\$20.00*	\$26.00*	—	—	—	—
Metropolitan Casualty Company	—	\$20.00	—	\$40.00	\$60.00	\$70.00	\$60.00	\$40.00

*Less 20 per cent, if earned

of this company in this state is good. As has been mentioned, their suit experience in Essex County is very high.

The *United States Fidelity and Guaranty Company* (assets, \$30,000,000) has not had a high suit rate in Essex County. They retain the law firm of Powers and Hall, in Boston, who have had a wide experience in defending malpractice suits. In their policy they have a dissolve attachment bond feature. Dr. Allen says that their record in this work is good. This company advises minimum limits of \$10,000-\$30,000, and believes so strongly that these limits are necessary that it does not write for less. On the other hand, the Medical Protective Company believes that \$5000-\$15,000 limits are sufficient, and will not write for more in Essex County.

The *American Motorists Company* (assets, \$10,000,000), a subsidiary of the Lumbermens Mutual Insurance Company (assets, \$41,000,000), is relatively new in the medical-defense field, although they have been in Massachusetts for ten years and now collect \$13,000 in premiums for this type of insurance. They advise \$10,000-\$30,000 limits, but will write for less.

The *Metropolitan Casualty Company* (assets, \$11,000,000) has been official for the Massachusetts Dental Society for nearly twenty-five years. A prominent feature of their policy provides payment of premium on appeal bonds without limit. This company pays \$15 a day for not more than seven days to the defendant doctor for loss of time while in court.

While this study was in progress, and after one set of rates had been offered, Ladd and Milne, in Haverhill, obtained the following concession from the American Motorists Insurance Company, which they represent: for all physicians in Essex County, whether engaged in general practice, major surgery or another specialty, but excluding those physicians using x-ray and radium for therapeutic purposes, the premium of \$20.00 for \$5000-\$15,000 limits is offered; for \$10,000-\$15,000 limits, \$24.00; and for \$10,000-\$30,000 limits, \$26.00. The company states that if a substantial amount of the business in this county is obtained over a period of one year, the rate will continue. No assessment can be made against the policyholder, and a dividend of 20 per cent, if earned, is returned to him. It is a legal reserve stock company, but is owned and operated by the Lumbermens Mutual Insurance Company. According to Ladd and Milne, the company offers this rate schedule only through their agency.

In summary, this committee chooses to recommend no one company for all the members. It is hoped that from

siderable importance, and a reasonable rate is desired.

The committee will gladly assist any member by allowing him to examine any of the data and all the letters that we have collected as a result of this investigation.

GUY L. RICHARDSON, M.D., *Chairman*
GEORGE J. CONNOR, M.D.
ALDEN B. GEORGE, M.D.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATHS

COTTON — CURTIS B. COTTON, M.D., of Wolfeboro, died August 6. He was in his seventy-eighth year.

Dr. Cotton, the son of Joel F. and Elivna (Gilman) Cotton, was born in Moultonboro and graduated from the University of Vermont College of Medicine in 1888. He was a member of the New Hampshire Medical Society and the American Medical Association.

He is survived by his widow, a son and a sister.

ROWE — ARTHUR J. ROWE, M.D., of Pennacook, died September 9. He was in his seventy-fifth year.

Born in South Barnstead, the son of Dr. James W. and Emma (Clark) Rowe, Dr. Rowe received his degree from Dartmouth Medical School in 1899. He was a member of the New Hampshire Medical Society and the American Medical Association.

He is survived by his widow, Mrs. Ida (Avery) Rowe, three brothers and a sister.

WAR ACTIVITIES

PROCUREMENT AND ASSIGNMENT SERVICE

The following release was recently received from the Washington office of the Procurement and Assignment Service:

The Directing Board of the Procurement and Assignment Service is pleased to announce that 95 per cent of the 1942 procurement objective of medical officers for the armed forces has already been met. Toward this total a number of states have supplied more than their share of physicians. Only a few states are lagging behind in their quotas, and it is from these states that the additional physicians needed during the current year should come.

The recruitment of such a large number of physicians in a few months is a remarkable achievement and another demonstration of the traditional patriotism and unselfishness of the medical profession. In this achieve-

ment, and particularly in those of its members who are "in service," the profession can justifiably take pride

The end, of course, is not yet. Increases in the armed forces will necessitate more medical officers, and additional demands will be made upon the profession for medical services in critical war-production areas. The Directing Board is convinced, however, that the physicians of this country will respond to future calls for service, whatever they may be, in the same splendid manner with which they have already volunteered for service with the armed forces.

FRANK H. LAHEY, M.D.

HAROLD S. DIEHL, M.D.

HARVEY B. STONE, M.D.

JAMES E. PAULLIN, M.D.

C. WILLARD CANALIER, D.D.S.

of the Massachusetts Hospital Association, accepted the cup in behalf of the hospitals that participated in the observance.

On their return to Boston, Dr. Wilinsky and Mr. R. F. Cahalane, executive director of the Blue Cross, whose organization directed the program, were received by Governor Saltonstall, who stated: "It is a great honor for the hospitals of Massachusetts to be singled out among those of the entire country for this national award. It only serves further to confirm my belief that the hospitals of the Commonwealth will continue to administer in wartime, as in peacetime, to the needs of the civilian population."

The cup will remain the permanent property of the two organizations, and is on view at the Blue Cross headquarters, 230 Congress Street.

MISCELLANY

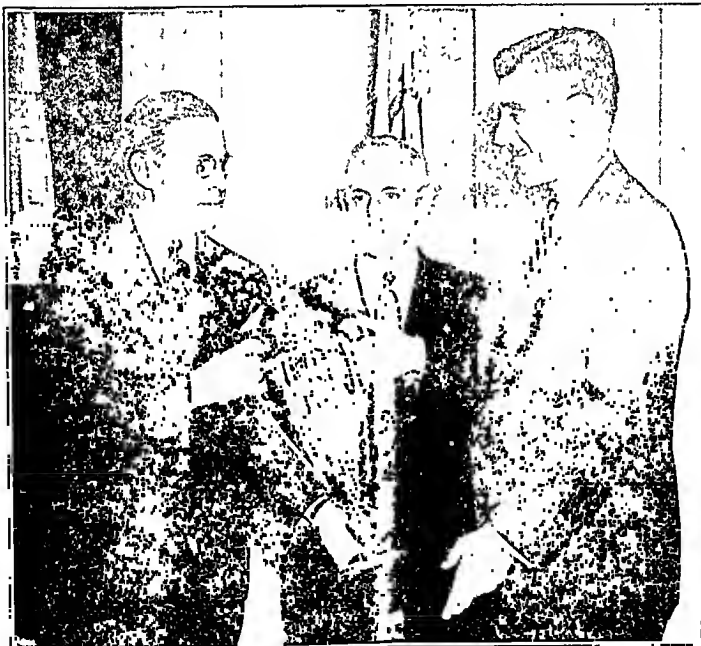
NATIONAL AWARD TO MASSACHUSETTS HOSPITALS

The American Hospital Association, at its recent meeting in St. Louis, awarded to the Massachusetts Hospital Association and to the Blue Cross a silver cup in recogni-

CORRESPONDENCE

NAVAL MEDICAL OFFICER PROCUREMENT

To the Editor: A recent letter received from the Navy Department directs the Office of Naval Officer Procurement not to accept applications for commissions in the



MASSACHUSETTS HOSPITALS GET NATIONAL AWARD

Governor Saltonstall views the cup that was awarded by the American Hospital Association to the Massachusetts Hospital Association and the Blue Cross for the best statewide observance of National Hospital Day. Holding the cup with the Governor is Mr. R. F. Cahalane and in the center is Dr. Wilinsky.

tion of the best state-wide observance of National Hospital Day on May 12. Dr. Charles F. Wilinsky, president

Medical Corps, United States Naval Reserve, from physicians of the New England States other than Massachusetts,

as the other states have met their quotas set by the Procurement and Assignment Service, War Manpower Board.

This directive also informs us that we should procure as many physicians from Massachusetts as possible, rejecting only those who have not been cleared by the Procurement and Assignment Service, those not meeting the professional requirements, and those with physical defects that, in the opinion of the Senior Medical Officer, would constitute a liability to the Government.

Those physicians from states other than Massachusetts who have *already been cleared* as available for military service will have their applications forwarded.

LIEUTENANT COMMANDER ROBERT S. PALMER, (MC) USNR
Senior Medical Officer

150 Causeway Street
Boston

MASSACHUSETTS LABORATORY TECHNOLOGISTS RESERVE CORPS

To the Editor: At the suggestion of medical and hospital authorities of the Massachusetts Committee on Public Safety, the Massachusetts Technologists Reserve Corps — consisting of approximately three hundred and fifty women trained as hospital technologists — is being organized under the direction of a special committee. The one hundred and twenty-four emergency (casualty receiving) hospitals in Massachusetts will be assigned technicians up to the needs of each hospital, sometimes as many as three or four, for specialized work in the event of civil disaster; at present, there is a serious shortage of adequately trained laboratory technologists.

The organization of the corps will be somewhat like that of a military group, with state, regional and local heads. A chief medical technologist will be assisted by subordinate technologists, and technicians' aides will be enrolled in the near future. All members will wear standard insignia on their regulation laboratory uniforms.

The corps will be established by a special committee appointed by Dr. A. William Reggio, Medical Director of the Massachusetts Committee on Public Safety. Nine regional directors will be in charge of enrollment in their respective areas.

The personnel of the corps will be recruited from women who have had experience or are currently employed in hospitals, public-health laboratories, technical work for private physicians, industrial hygiene or pharmaceutical houses. They will be urged to spend two or three hours a week in refresher courses, unless they can demonstrate that they are already fully qualified for such work.

The regional directors, to whom inquiries concerning the corps should be addressed, are as follows:

- Region 1. Dr. Helen M. Scoville, 741 North Street, Pittsfield
- Region 2. Dr. Fred D. Jones, 20 Maple Street, Springfield
- Region 3. Dr. James S. P. Beck, 119 Belmont Street, Worcester
- Region 4. Dr. D. A. Nickerson, Salem Hospital, Salem
- Region 5. Dr. Charles F. Branch, 750 Harrison Avenue, Boston
- Region 6. Dr. Helmuth Ulrich, 99 Bay State Road, Boston
- Region 7. Miss E. K. Jones, Supt., Cape Cod Hospital, Hyannis
- Region 8. Dr. Isabel M. Wason, 101 Page Street, New Bedford
- Region 9. Dr. Edwin St. John Ward, Templeton

The co-operation of all physicians in the Commonwealth is requested to make this program effectual, and it is hoped that physicians who know of potential laboratory technicians will refer them to the proper regional directors.

DONALD A. NICKERSON, M.D., *Chairman*
Laboratory Technician's Committee

Salem Hospital
Salem, Massachusetts

NOTICES

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM, NOVEMBER

- Tuesday, November 3 — Some Problems in Malaria. Dr. Edward I. Salisbury.
- Wednesday, November 4 — Dermatological clinic. Dr. Francis M. Thurmon.
- Friday, November 6 — Changes in Chloride Metabolism. Dr. George W. Thorn.
- Friday, November 13 — Selected Problems in Aviation Medicine. Dr. Ross A. McFarland.
- Wednesday, November 18. Peptic Ulcer. Colored motion picture — courtesy of John Wyeth and Brother, Incorporated.
- Friday, November 20 — Clinicopathological conference. Dr. Chester S. Keefer and Dr. H. E. MacMahon.
- Wednesday, November 25 — Treatment of Tuberculosis. Dr. Joseph H. Pratt.

On Tuesday and Thursday mornings (except November 3) Dr. S. J. Thannhauser will give medical clinics on hospital cases.

MASSACHUSETTS PSYCHIATRIC SOCIETY

The annual meeting of the Massachusetts Psychiatric Society will be held at the Hotel Kenmore, Boston, on Monday, November 9, at 6:30 p.m. The guest speaker will be Dr. Edward A. Strecker, professor of psychiatry, University of Pennsylvania, whose topic will be "Treatment of Neuropsychiatric Disabilities."

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, November 3, at 8:15 p.m.

PROGRAM

Present Status of Sex-Hormone Therapy. Dr. Joseph C. Aub. Discussion by Drs. H. B. Friedgood, Samuel Gargill and Henry Finkel will follow.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination and review of case histories (Part I) for all candidates will be held in various cities of the United States and Canada on Saturday, February 13, 1943, at 2:00 p.m.

Arrangements will be made so far as possible for candidates in military service to take the Part I examination (written paper and submission of case records) at their places of duty, the written examination to be proctored by the commanding officer (medical) or some responsible person designated by him. Material for the written examination will be sent to the proctor several weeks in advance of the examination date. Case records may be submitted in advance of the above date only by candidates in

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TETANUS TOXOID IMMUNIZATION OF ADOLESCENTS*

Skin Reactivity, Allergy and Unfavorable Reactions

J. ROSWELL GALLAGHER, M.D.,† CONSTANCE D. GALLAGHER, B.A.,‡ AND GUSTAV G. KAUFMANN, M.D.§

ANDOVER, MASSACHUSETTS

PROPHYLAXIS against tetanus is of special interest to physicians who deal with adolescents. Members of that age group, because of their athletic and other activities, suffer frequent minor injuries, and the question of whether or not to give tetanus antitoxin prophylactically arises repeatedly; one must frequently choose between the dangers, discomforts and horse-serum sensitization of tetanus antitoxin and the possibility of tetanus following an apparently trivial wound. The present development of tetanus toxoid, reports of its efficiency in producing a protective level of antitoxin in the recipient's serum, and evidence that its administration is only rarely accompanied by unfavorable reactions appear to have solved, to a considerable extent, the problem of tetanus prophylaxis.

Inevitably, when the widespread use of a new prophylactic measure is suggested, attention becomes focused, and usually to an unreasonable extent, on the frequency and degree of unfavorable reactions produced by that agent. Hall,¹ in reporting the results of immunizing 2300 midshipmen, states that only 1 developed urticaria, only 2 had fever and malaise, and only 8 complained of sore arms after the first dose of alum precipitated tetanus toxoid; following the second dose, 1 case of anaphylactic shock, 4 cases of urticaria and 38 sore arms developed. During the following year, 793 men were immunized with a different preparation of toxoid, and an unfavorable reaction occurred in only 1 case. Whittingham,² in reporting the immunization of 61,000 men in the Royal Air Force, states that only 5 had malaise and fever and that 9 developed urticaria. A group of 186 allergic children, ranging from three to fifteen

years of age, were immunized by Peshkin,³ without any disturbing reactions; only 2 had a brief elevation in temperature.

The various objectionable features of tetanus antitoxin and the low incidence of unfavorable reactions from tetanus toxoid in such groups as those mentioned above, together with the apparent efficiency of toxoid in raising the serum antitoxin to a protective level, made us urge the parents of a group of adolescents under our care to have them actively immunized against tetanus. Extensive experience in the use of tetanus toxoid among adolescents is apparently lacking, and because of the frequency of unfavorable reactions from diphtheria toxoid in this age group, we approached our project more conservatively than the experience of others with different age groups seemed to justify.

Rogers⁴ has emphasized the desirability of this immunization for all allergic children, in whom the reports of Peshkin³ and Unger⁵ indicate that unfavorable reactions are uncommon. However, recent orders from the War Department⁶ suggest that allergic persons be skin tested and, if the skin test is positive, be given tetanus toxoid in divided doses; to be ultraconservative and also to determine the skin reactivity to toxoid in those persons both with and without an allergic history, we decided to test each boy in our series prior to each immunizing dose of tetanus toxoid. The results of these skin tests, the incidence of unfavorable reactions and the relations between these skin tests, reactions and various allergic states are reported.

METHOD

Permission to give tetanus toxoid was obtained from the parents of about 500 boys, who ranged in age from thirteen to nineteen years. Alum precipi-

*From the Department of Health, Phillips Academy. This study was aided by a grant from the Carnegie Corporation.

†School physician, Phillips Academy.

‡Research associate, Phillips Academy.

§Assistant school physician, Phillips Academy.

tated toxoid in two doses of 1 cc. each was given; the interval between doses ranged from four to seven weeks. Prior to each dose, 0.1 cc. of a 1:10 physiologic saline dilution of the tetanus toxoid was injected intradermally, and after an interval of ten minutes, the skin reaction was recorded; in the rare cases in which the skin reaction was very strongly positive, the undiluted toxoid was given in divided doses—0.1, 0.2, 0.3 and 0.4 cc.—on four successive days. The degree of "sore arm" and of malaise, as recorded, was based on questions directed to each boy, and was obviously greatly influenced by the boy's personality as well as by our interpretation of his statements.

RESULTS

Table 1 presents the results of skin testing with a 1:10 physiologic saline dilution of tetanus toxoid that was injected intradermally before the first

TABLE 1. *Results of Skin Tests before Tetanus Toxoid Immunization.*

REACTION	NO. OF CASES	PERCENTAGE OF TOTAL
Negative	373	73.3
Less than 10 mm. in diameter (\pm)	95	18.7
10 to 20 mm. (+)	22	4.3
20 to 30 mm. ($++$)	6	1.2
30 mm. or more ($+++$)	13	2.5
Total	509	

immunizing dose was administered. Eight per cent of the entire group showed a skin reaction measuring 10 mm. or more in diameter, and 3.7 per cent showed a strongly positive ($++$ or $+++$) reaction.

Table 2 lists the incidence of asthma, hay fever, previous tetanus antitoxin prophylaxis and hay fever or asthma prophylactic therapy in each group. The large percentage of boys who had

tetanus-antitoxin prophylaxis or allergy and only 5 of the 19 who had strongly positive skin tests gave a history of asthma or hay fever. The fact that 23 per cent of the $+++$ reactors had asthma is worthy of attention, but this seems less significant in view of the large number of those with asthma who had negative skin tests. It is of interest that of the 10 students who regularly received some sort of allergy prophylaxis, only 1 had an initial skin test with diluted tetanus toxoid greater than 20 mm. in diameter.

Table 3 shows clearly that the highest percentage of students having a history of various allergic states or previous prophylaxis always fell in the group with negative skin tests and that only relatively small percentages of each of these had strongly positive reactions.

The changes in skin reactivity following the inoculation of the first 1-cc. dose of tetanus toxoid and measured just before the administration of the second prophylactic dose were recorded. The entire group was not given a second skin test, but no boy whose first test was positive was omitted. Negative skin tests were recorded at both times in 318 cases; 109 others had approximately the same degree of reaction at both the first and second skin tests. In 10 cases, the first skin test measured less than 20 mm., and the second test was recorded as negative; second tests were recorded as $+$ in 10 subjects whose initial tests were negative. Three boys whose initial skin test was recorded as $++$ had at their second test a \pm reaction, and 9 whose initial skin test was \pm had a skin test of $++$ or $+++$ following their first immunizing dose of toxoid; in only these last 12 cases (2.6 per cent), was there a significant change in skin reactivity subsequent to the inoculation of an immunizing dose of tetanus toxoid. Of the 9 boys whose initial skin test was \pm or nega-

TABLE 2. *Incidence of Asthma, Hay Fever and Previous Tetanus and Allergy Prophylaxis according to Reactions.*

REACTION TO SKIN TEST	TOTAL NO. OF CASES	NO HISTORY OF ALLERGY OR PREVIOUS PROPHYLAXIS		HISTORY OF ASTHMA		HISTORY OF HAY FEVER		PREVIOUS TETANUS PROPHYLAXIS		PREVIOUS ALLERGY PROPHYLAXIS	
		NO. OF CASES	PERCENT-AGE	NO. OF CASES	PERCENT-AGE	NO. OF CASES	PERCENT-AGE	NO. OF CASES	PERCENT-AGE	NO. OF CASES	PERCENT-AGE
Negative	373	245	65.7	13	3.5	45	12.1	84	22.6	5	1.4
\pm	95	61	64.2	3	3.1	21	22.1	18	18.9	3	3.1
$+$	22	14	63.7	2	9.1	2	9.1	6	27.3	1	4.5
$++$	6	2	33.3	0	0	0	0	4	66.7	0	0
$+++$	13	5	38.4	3	23.1	2	15.4	3	23.1	1	7.7
Totals	509*	327		21		70		115		10	

*The total number of cases (509) does not correspond to the total number of histories (543) since many of the boys were classified in more than one group.

been given tetanus antitoxin in the past is interesting, but the most significant fact is that about 36 per cent of the group that was strongly positive to the skin tests gave no history of previous

tive and whose second test was $++$ or $+++$, 1 had asthma, 5 had hay fever, and 2 of these and 1 other had been given tetanus antitoxin in the past; 2 of these 9 boys had neither

an allergic history nor a previous dose of tetanus antitoxin. Fifteen boys were given tetanus toxoid in divided doses on the basis of strongly positive

was omitted. No anaphylactic reactions occurred: 3 boys "felt faint" directly following their inoculations, but their apprehension and pallor before in-

TABLE 3. Incidence of Reactions according to History.

History	TOTAL NO OF HISTORIES	-		±		+		++		+++	
		NO OF CASES	PER CENT AGE	NO OF CASES	PER- CENT- AGE	NO OF CASES	PER- CENT- AGE	NO OF CASES	PER- CENT- AGE	NO OF CASES	PER- CENT AGE
No history of allergy or previous prophylaxis	327	245	74.9	61	18.7	14	4.3	2	0.6	5	1.5
History of asthma	21	13	61.9	3	14.3	2	9.5	0	—	3	14.3
History of hay fever	70	45	64.2	21	30.0	2	2.9	0	—	2	2.9
Previous tetanus prophylaxis	115	84	73.0	15	15.7	6	5.2	4	3.5	3	2.6
Previous allergy prophylaxis	10	5	50.0	3	30.0	1	10.0	0	—	1	10.0
Totals	543	392		106		25		6		14	

skin reactions; in 11, the initial and second skin tests were approximately the same; in 4, the skin reactivity at the time of the second test was recorded as +.

Table 4 shows that only about 16 per cent of the boys who had strongly positive skin tests complained of very sore arms or any malaise after

TABLE 4. Incidence of Effects following Both the First and Second Immunizing Doses of Toxoid according to the Degree of Skin Reactivity before the First Dose

EFFECT	TOTAL NO OF CASES	NO OF CASES					
		-	±	+	++	+++	
Sore arms							
Slight	64	48	12	0	0	3*	
Moderate	27	14	6	3	1	4*	
Malaise							
Slight	17	13	0	1	0	3*	
Moderate	2	1	1	0	0	0	
Admitted to infirmary	12	9	3	0	0	0	
After first dose	4	4	0	0	0	0	
After second dose	8	5	3	0	0	0	
Sterile abscess†	2	2	0	0	0	0	
Urticaria‡	1	0	0	0	0	1§	
Anaphylactic reaction	0	0	0	0	0	0	

*Two boys in this group were given toxoid in divided doses

†After each dose

‡Urticaria also following the second skin test, second immunizing dose not given

§This boy was given toxoid in divided doses

the first dose of toxoid, and that a moderate number of those who had similar complaints had negative skin tests.

Of the 12 boys admitted to the infirmary because of headache, malaise and fever, all of about twenty-four hours' duration, none had a positive skin test. Two boys, whose skin tests were negative, developed sterile abscesses at the site of injection a few days following both the first and second inoculations. Another, whose skin tests were strongly positive, developed giant urticaria after his first inoculation, given in divided doses; the second skin test was followed within four hours by the development of giant urticaria (which responded to adrenalin), and the second immunizing dose

inoculation indicated that these reactions were psychogenic.

Table 5 presents the incidence of unfavorable reactions among boys with a history of hay fever or asthma, or both, as compared with the reactions in those without history of allergy. It is obvious that there was no striking difference in the incidence of reactions in the two groups.

DISCUSSION

Our experience and that of many others clearly indicate that immunization with tetanus toxoid is a practical, safe and very desirable procedure; immunization at an early age and in combination with diphtheria antitoxin appears to be the method of choice, but our results indicate that the use of tetanus toxoid is satisfactory during adolescence.

The relatively high incidence of unfavorable reactions from diphtheria toxoid during adolescence and our belief that results obtained in other age groups should not be applied without careful investigation to adolescents were factors that interested us in the skin reactivity of this group to diluted tetanus toxoid. Because of the hesitancy of some physicians to give this prophylaxis to allergic persons, who obviously need it most, and because of recent War Department orders to proceed with caution in the immunization of all allergic persons, it is interesting that skin sensitivity to diluted tetanus toxoid is far from limited to members of the group having a history of allergy, and that although about 38 per cent of those having strongly positive skin tests had either asthma or hay fever, only about 14 per cent of those with asthma had strongly positive skin tests. Local and systemic reactions were no more frequent among those with positive skin tests to tetanus toxoid than among those who did not exhibit such sensitivity, but these results may have been affected by our procedure in giving divided doses to strongly positive subjects. A significant number (36 per cent) of boys with strongly positive skin tests gave no allergic history, and a considerable

number of those who had unfavorable reactions had both a negative skin test and a negative allergic history; it appears that neither skin reactivity to tetanus toxoid nor history of previous allergic manifestations is a reliable indicator of the

SUMMARY

Five hundred and nine boys ranging from thirteen to nineteen years of age were given two immunizing doses of tetanus toxoid without subsequent development of serious local or systemic

TABLE 5. Comparison of Unfavorable Reactions Occurring in Boys with and without a History of Allergy.

	TOTAL NO. OF CASES	SORE ARMS		MALAISE		INFIRMARY ADMISSION		ABSCESS NO. OF CASES	URTICARIA NO. OF CASES
		NO. OF CASES	PER- CENT- AGE	NO. OF CASES	PER- CENT- AGE	NO. OF CASES	PER- CENT- AGE		
History of allergy.	75	16	21.3	3	4.0	2	2.7	0	0
No history of allergy	434	75	17.0	16	3.7	10	2.3	2	1
Totals	509	91		19		12		2	1

possibility of local or systemic reaction. Fortunately, no anaphylactic reactions were encountered in this group; one can only speculate whether anaphylactic or other reactions might have developed in any of the 15 boys whose skin tests were strongly positive had they been given full instead of divided doses of tetanus toxoid, but we do know that unfavorable reactions were negligible, except for 1 case of urticaria in this group. Four boys who had ++ skin tests were given full doses of toxoid: none of them had immediate unfavorable reactions, and none subsequently complained of sore arms or required admission to the infirmary, and only one complained of slight malaise. It seems necessary, before either the value of skin testing or the desirability of giving small divided doses to persons positive to the skin test can be determined, to investigate further the relation of anaphylactic or other severe reactions to skin sensitivity to toxoid and the incidence of severe reactions in strongly positive tests when toxoid is administered in full rather than divided doses. On the basis of our experience, the conservative and safe procedure in immunizing members of the adolescent age group is to precede the inoculation of tetanus toxoid by a skin test; little time or effort can be lost by this procedure, and until a more extensive experience with adolescents is available, conservatism is certainly commendable. Our results indicate that in only a small number of cases did initial mild skin reactions change to more strongly positive ones following the administration of the first dose of toxoid, and unless one is to be ultraconservative, a skin test prior to the second immunizing dose is hardly indicated.

reactions; the incidence of unfavorable reactions, however, was apparently higher in this group than among either younger or older subjects.

Strongly positive skin tests to diluted tetanus toxoid were recorded in 3.7 per cent of the group; 1 case of urticaria occurred, 2 sterile abscesses developed, and 12 subjects had sufficient malaise and fever to warrant infirmary care for twenty-four hours.

There is apparently little relation between known previous allergic states and skin sensitivity to diluted tetanus toxoid.

Neither skin sensitivity to diluted tetanus toxoid nor elicited previous history of allergic manifestations was found to be a reliable criterion on which to predict skin sensitivity or the development of unfavorable local or systemic reactions.

Fifteen of the 19 boys whose skin tests were strongly positive were given toxoid in four divided doses; no unfavorable reactions occurred in this group.

Until further experience with this age group is evaluated, it is suggested that skin tests with diluted tetanus toxoid be made prior to the administration of each immunizing dose.

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ADEQUATE CLINICAL RECORDS—A PROFESSIONAL RESPONSIBILITY*

JOSEPH H. PRATT, M D T

BOSTON

IT is a fact as remarkable as it is disturbing that physicians on the whole do not realize the value of medical records of the patients under their care. This neglect is all the more surprising because leading medical teachers have by precept and example emphasized the value of the clinical history and of careful observations made at the bedside. The injunction to observe, to record and to analyze has often been made. It is necessary to have as good medical records in a small hospital as in a large one because the patient presents the same problems in each; he is entitled to thorough study and his record should be written promptly, accurately and completely.

Dr. Malcolm T. MacEachern,¹ director of hospital activities of the American College of Surgeons, states: "Prior to the commencement of the hospital standardization program in 1915, only a limited number of hospitals in the United States, less than one hundred, kept medical records of an acceptable type. The remainder of the hospitals had scant information other than that found in the nurses' notes." The minimum standards established twenty-four years ago by the American College of Surgeons and efforts to secure its enforcement have resulted in some improvement, but much remains to be done. Clause 4 of the minimum standard relates to medical records; it states, "that accurate and complete records be written for all patients and filed in an accessible manner in the hospital." It defines a complete medical record as one that includes identification data, complaint, personal and family history, history of the present illness, physical examination, special examinations, provisional or working diagnosis, medical or surgical treatment, gross and microscopic pathological findings, progress notes, final diagnosis, condition on discharge, follow-up and, in fatal cases, autopsy findings. Unfortunately, many hospitals—even some of those approved by the American College of Surgeons—keep records that are far from satisfactory. The fault lies in the failure of the members of the medical staff of the hospital to become "record conscious." Much of the blame can be traced back to the clinical teachers in the medical schools, who did not instill into the minds of their students the necessity of keeping detailed records if they are to do justice to themselves or to their patients.

Hippocrates,² in the dawn of history, recorded as accurate observations as were possible at that time and made daily progress notes in acute cases. An example, selected almost at random, is Case 4 from the 26 cases he collected for his third book on epidemics.

In Thasus, Philistes had headache of long continuance, and sometimes was confined to bed with a tendency to deep sleep, having been seized with continual fevers from drinking, the pain was exacerbated, during the night he at first became hot. On the first day he vomited some bilious matter, at first yellow, but afterwards of a verdigris green color and in greater quantity, formed feces passed from the bowels, passed the night uncomfortably. On the second day, deafness, acute fever, retraction of the right hypochondrium, urine thin, transparent. On the third in an uncomfortable state. On the fourth, convulsions. All the symptoms exacerbated. On the fifth early in the morning, died.

This record presents clearly and objectively, four hundred years before the birth of Christ, what appears to be a fulminating case of meningitis. There is great need today of cultivating this ancient diligence of Hippocrates in the recording of medical cases.

Laennec, the greatest name in medicine after Hippocrates, based his epoch-making work in auscultation on his records of detailed physical findings and his autopsy notes in diseases of the chest.

As an illustration of how bad records are today, I cite the following recent experience. I saw a patient on the eighth day of her illness and made the following note:

February 17, 1942 Mrs. S. K., aged 31. Complaints of frequent chills and fever.

Present illness. Onset with a sore throat on February 10. The next day cough began and she had a tight feeling behind the sternum. On the night of February 12, she awoke feeling very hot, she took her temperature and found it to be 102.5°F. Doctor called the morning of February 13, examination of the chest was negative, but the temperature was not taken. The patient raised much greenish sputum on the following day, previously, the cough had been dry. She had a series of shaking chills lasting half an hour or so beginning on the night of February 14, followed by a sense of great heat. On February 15, the temperature reached 101.5°F. Yesterday morning about 7 o'clock, it was 100°F. At 11:30, it was 98.6°F. At about 4 p.m., the temperature was 103.5°F. A shaking chill occurred in the middle of the night.

Examination of the chest was negative. Although the oral temperature at the time of examination

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¹Professor of clinical medicine, Tufts College Medical School, physician-in-chief, New England Medical Center.

was 101.1°F., the respirations were only 16. There was no leukocytosis, and the urine was normal. It was evident that this was an unusual case that demanded careful study for a correct diagnosis. The patient was sent to an excellent small hospital in a neighboring town where resident physicians, a full-time roentgenologist and a pathologist were on the staff.

The history of the present illness, taken by a salaried resident physician, was as follows: "Chief Complaint: Chills and fever. Burning on urination. Date of onset week today, which began as a heavy chest cold." No attempt at a record would have been better because two of the three state-

be the correct diagnosis. The resident, of course, learned nothing from his so-called "study" of the case. Because this history was the worst I think I have ever read in my experience of forty-seven years, I interviewed the young man and found that he had graduated from an unrecognized school, where he had had no practical instruction or experience in case taking. He had served an internship in a large hospital, where he had had a large experience in case taking, but his clinical histories had been accepted without correction and his records had never been supervised by the attending physicians.

A pleasing contrast to the unsatisfactory state of medical records in many hospitals of New England today is presented by an examination of the medical records of the Massachusetts General Hospital made over a hundred years ago (Fig. 1).

This hospital was opened in September, 1821. Since that date, the records have been carefully preserved. The first 50 cases were bound to form Volume 1 of the medical records. For about a hundred years thereafter, each series of 50 cases was bound in a separate volume. These early case reports are worthy of study. The history of the very first case was written out in detail (Fig. 2). The careful penmanship attests to the value attached to the clinical record. I have read that the physician's notes were copied for the official record by the hospital apothecary, who wrote a fine hand. James Jackson was the physician-in-chief. His opinion of the worth of medical records is attested by his own statement:

It has been the practice at the Massachusetts General Hospital, in the medical department, to note the state of the patient every day, in acute cases, as our records show. It has been our intention to inquire into the state of all the functions in the beginning of each case, and more or less fully from day to day. But we have been willing to diminish the labor of our records by mentioning only the functions which manifested disease, while oftentimes we made no records of those which appeared healthy. Unless it was certain, however, that this course was uniformly pursued, it is obvious that there must be some uncertainty in any given case, whether something had not been omitted. There is no doubt that our negligences have been so frequent that our records cannot be relied on, except for what is positively stated. Nor can we say that our inquiries have been sufficiently full originally. We have often failed in learning and still oftener in stating the previous histories of our patients. . . . In the first years we were the most deficient, but we have made our observations with more and more care as we have proceeded.

He wrote these words in his classic report on typhoid fever,³ communicated to the Massachusetts Medical Society in 1838.

Where did Dr. Jackson get his conviction of the significance of hospital records, which possessed

1	James J. Bennett	Dec 12 29	Chills
2	William H. H.	20 25	Chills
3	Joseph B. B.	20 30	Chills
4	Samuel B. B.	20 31	Chills
5	Charles B. B.	25 41	Chills
6	William B. B.	26 34	Chills
7	John B. B.	27 28	Chills
8	John B. B.	29 23	Chills
9	John B. B.	Dec 5 24	Chills
10	John B. B.	20 31	Chills
11	John B. B.	20 22	Chills
12	John B. B.	20 22	Chills
13	John B. B.	20 22	Chills
14	John B. B.	20 22	Chills
15	John B. B.	20 22	Chills
16	John B. B.	20 22	Chills
17	John B. B.	20 22	Chills
18	John B. B.	20 22	Chills
19	John B. B.	20 22	Chills
20	John B. B.	20 22	Chills
21	John B. B.	20 22	Chills
22	John B. B.	20 22	Chills
23	John B. B.	20 22	Chills
24	John B. B.	20 22	Chills
25	John B. B.	20 22	Chills
26	John B. B.	20 22	Chills
27	John B. B.	20 22	Chills
28	John B. B.	20 22	Chills
29	John B. B.	20 22	Chills
30	John B. B.	20 22	Chills
31	John B. B.	20 22	Chills
32	John B. B.	20 22	Chills

FIGURE 1.

ments made were false and hence misleading: the patient had had no burning on urination, and she had not had a chest cold.

On inquiry, I found that there was no supervision of this resident's records. The history as I have given it stands as the official record. The case history as given by me was typical of virus pneumonia, a disease that has only recently been recognized and presents a striking and characteristic clinical picture. This was subsequently proved to

him when he first took charge of the medical work at the hospital in 1821? Doubtless, the answer is, From his teachers in Great Britain, where he "walked" the hospitals of London and Edinburgh in 1800. It seems evident that the case records of these British hospitals must have been good and

diseases and the present illness, we have the testimony of James Jackson⁴ that Louis made and recorded more thorough observations than any of his predecessors

He noted the actual phenomena present at his examination, depending for this not only on the statement of the patient, but on his own senses, his eyes, his ears, and his hands—he was not satisfied with noting the functions, in which the patient complained of disorder, but examined carefully as to all the functions, recording their state as being healthy or otherwise, and even noticing the absence of symptoms which might bear on the diagnosis

I have heard Osler refer to Louis as the patron saint of the Massachusetts General Hospital, but it was not the influence of Louis that first led James Jackson to keep good records from the opening of the hospital. This is a known fact, since Jackson has left on record the statement that he first learned of Louis's work in 1830. This was nine years after the opening of the hospital. His later debt to Louis, he freely acknowledged. The value of making and recording the physical examination in the manner outlined above, was taught him by Louis. In the first case admitted to the hospital, there was not a single entry on the objective symptoms and signs presented by the patient at the time of his entry, the record dealing solely with the present and past history. This defect was soon remedied, and it was not long before careful notes were made of the objective findings.

In the summer of 1833, James Jackson, Jr, then twenty three years of age, returned to Boston after nearly two years of study in Paris, carried on chiefly under the direction of Louis. On the morning of October 15, 1833, young Jackson went to the Massachusetts General Hospital, where he examined a patient ill with typhoid fever, who had been admitted on the previous evening to his father's service, and recorded the following notes on the case (I give them in full as they furnish convincing evidence that the quality of this medical record, made one hundred and eight years ago, and the care and thoroughness of the observations were of a high order)

October 15, 1833—S K, aet. 32, unmarried, eyes, hair and complexion dark, maid servant, born in Salem. Entered the hospital last evening ill since seventh instant, perfectly well before, on that day headache, distress and pain in limbs, anorexia, weakness, obliging her to go to bed. Since then she has had bad taste in mouth, no soreness of throat, nor dysphagia, thirst, anorexia, nausea after taking too much liquid, but not at other times, diarrhoea from the first, four or five dejections a day, urine not observed, catamenia on 10th, lasting one day (they had occurred in order the week preceding), no chills, occasional

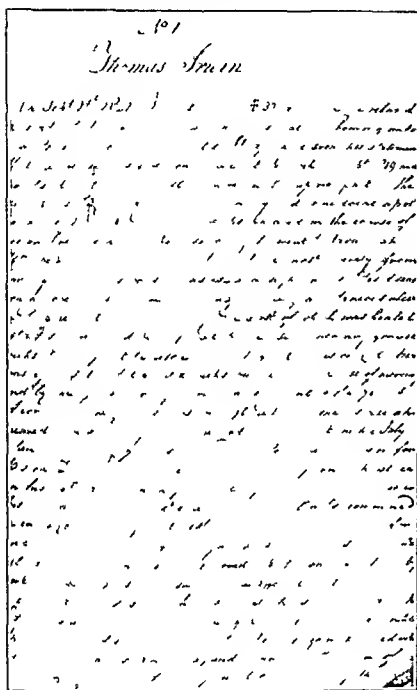


FIGURE 2

that he took them as a model when the Massachusetts General Hospital was opened. Additional evidence of the importance attached by Scottish hospital physicians to clinical records in the first half of the last century was the custom, introduced by them, of giving the name of the clinical clerk who made the record when they published the notes of the case in a medical paper.

It is of interest to discover and give credit to the physician who first taught and practiced the approved modern plan of making and recording a thorough clinical history and complete physical examination. I am convinced from my reading that this honor belongs to the great French physician, Pierre Charles Alexander Louis. In addition to a careful history of the family, the past

heat and sometimes sweat at night; no cough; nor dyspnoea, or very little of these; no pain in chest, nor palpitation; headache and dizziness; tinnitus aurium and deafness; no epistaxis; no sleep; some delirium. On the 10th she had the following: Rx. hydr. subm. jalap. 33 gr. viii—misce. After this some castor oil; and, the dejections, continuing too frequent, she had fifteen drops of tinct. of opium. After this she had not any important medicine.

The above details were partly from the physician who had attended her.

Now, October 15th, morning; — countenance, as well as mind, very stupid; memory treacherous; cannot tell how long she has been ill, though clear and positive as to existence, or non-existence of certain symptoms; features still, eyes fixed, looking melancholy; face pale or sallow, and evidently emaciated; since her entrance (five p.m. yesterday) no vomiting; great thirst of which only she has complained; two dejections, very watery, not dark, nor painful, quite offensive to smell, one of them a pint; through the night restless and watchful, and probably delirious, though silent, for she arose from bed and went to table for drink in absence of watcher, though she has seemed too feeble to rise up. Lips slightly dry; tongue dry, enlarged, protruded partially, a thin, brown coat over part of lobes; some soreness of gums, which have a white coat and give out a mercurial fetor; abdomen not swollen, nor painful, but a little tender on pressure at epigastrium; some small rose pimples on abdomen, but no sudamina; spleen not felt; skin hot and dry; pulse varies from 112 to 120, small, not soft; resp. 21, not difficult; no dilatation of alae nasi, but slight noise in nose; lies on right side.

How shall the pressing problem of obtaining adequate medical records in small hospitals, as well as large, be solved? Various means have been suggested and applied with success. It is essential that the medical staff be convinced of the necessity of good medical records; this is a matter of education. The reasons for keeping case records have been well stated by Musser⁵ as follows:

Records of cases should be kept for obvious reasons. The habit compels a general survey of the case, and tends to prevent oversight in the examination. It naturally aids in the training of the powers of observation. It teaches a precision in the narration of cases. The memory is aided by repetition and by lack of haste in ascertaining phenomena. The data are on record for more mature reflection, and to aid in the study of the literature of similar cases. The record is of value in case the patient returns for advice after a lapse of time. It may be of medico-legal value. The mental effect on the patient is good, for the taking of notes requires time and accurate, studied observation. In case it is desired to study a large number of cases, records are scientific data.

No patient is adequately cared for by the hospital physician until all information bearing on the case has been elicited and recorded. To do less is to neglect the patient. If the physician realizes this, he can no longer offer the excuse that he is too busy to write notes, for this is tantamount to

saying he is too busy to care properly for his patients. Notes do not have to be long to be adequate: a few sentences dictated at the bedside or at the operating table may be worth more than a page written the following day. Every hospital should, if possible, provide a secretary or a dictaphone.

In the preparation of the following suggestions MacEachern's¹ writings have been helpful.

1. Physicians might be convinced of the value of good clinical records if they were required on accepting an appointment to the medical or surgical staff, to sign a statement that they assume responsibility for seeing that all the records of patients under their care are written promptly and completely. This responsibility cannot be delegated to interns or residents.

2. Residents, if properly trained, are of great aid in providing good records, but their work should be supervised by the attending physician, who should always make and record his own observations. Otherwise, it is the record of the resident and not fair to either the physician or his patient.

3. A medical-records committee should be appointed. It is the duty of the chief-of-staff to see that this committee is active and efficient. It should review all records regularly, preferably weekly, and promptly refer back unapproved records to the responsible physician.

4. A medical-records librarian should be provided. She can judge the records quantitatively, if not qualitatively, and can furnish much aid to the medical-records committee.

5. Evaluation of the medical record should first be done by the attending physician. MacEachern says that the practice is increasing of having the attending physician sign a statement reading as follows: "This is to certify that I have carefully reviewed the attached record, . . . and to the best of my knowledge, I find it accurate and complete." He continues:

To do its work thoroughly and impartially the medical records committee must have the authority of the medical staff to make frank and unprejudiced appraisal of each record. It also has the responsibility of reporting to the medical staff, at each meeting regarding deficiencies. Medical records will only attain a proper standard of quality if they are actively reviewed in every hospital in a critical, constructive, and unbiased fashion at stated regular periods, and reports made systematically to the administration and the medical staff.

6. A medical audit may be carried out. This is based on an analysis of the discharge records of all patients and was devised by Dr. Thomas R. Ponton⁶; its introduction was aided by the Association of Record Librarians of North America.

I have observed its successful employment at the Thayer Hospital, Waterville, Maine, where it was introduced by Dr. Frederick T Hill. It is an additional aid in obtaining good medical records and may prove worthy of adoption by all hospitals.

During the last few years, earnest efforts have been made by laywomen serving as record librarians, as their published papers indicate, to devise means for making hospital physicians record conscious. Shades of Hippocrates, Louis and James Jackson! What a shock to these pioneers it would be to learn that the physicians of the present generation, who pride themselves on the high position attained by scientific medicine, have neglected the very foundations on which scientific

medicine rests—namely, the careful observation and recording of facts obtained by the unaided senses—the eyes, the ears and the hands—of the examiner. Physicians in small hospitals often lament the lack of laboratory facilities for special tests, but they still neglect the all important methods available to all.

30 Bennet Street

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THE DRUG THERAPY OF MIGRAINE HEADACHE*

LOWELL S. TROWBRIDGE, M.A.,† THODORE J. C. VON STORCH, M.D.,‡
AND MAJOR MERRILL MOORE, M.C., A.U.S.§

BOSTON

UNTIL recently, migraine headache has been most difficult to control. However, since the advent of ergotamine tartrate, this drug has been effective in aborting or terminating 90 per cent of the attacks in 600 cases.¹ In spite of such encouraging results, older and nonspecific drugs continue to be used by those suffering from migraine, probably because of ignorance on the part of the lay public concerning the existence of ergotamine tartrate. To compare the results obtained by specific (ergotamine tartrate) therapy and nonspecific therapy, the effects of various medications used by 200 patients were analyzed in terms of the patients' evaluation of the various drugs. Ergotamine tartrate was employed in the Out Patient Department of the Boston City Hospital. The other drugs were used by the patients on their own initiative or were prescribed by physicians outside the hospital. All the observations are subjective and were elicited directly from the patients.

The diagnosis of migraine was determined according to criteria previously specified by one of us.² The patients were asked to name the drug or drugs used by them to relieve their headaches and to evaluate the relief obtained.

The analysis of patients' reports on their experience with various therapies included only drugs that, in our opinion, had been used by the patient long enough to permit him to evaluate

them accurately. There were two steps in the analysis of the data: classification of drugs in groups according to their type or site of action, and a compilation of the number of patients who had used drugs in each group with their subjective opinion of the result of such use. Most patients had employed several—in some cases, as many as ten drugs—in their search for relief.

There were eight groups comprising forty eight different drugs that had been tried from time to time. Individual patients had used these drugs for

TABLE 1 Comparative Effect on Migraine Headache of Various Drugs

DRUGS	NO OF PATIENTS	EFFECT			
		INVASIVELY COM- PLETE RELIEF	EFF. QUANTITATIVE RELIEF	USUALLY IN- ADEQUATE RELIEF	INVASIVELY UN- TAINABLE RELIEF
Vasoconstrictors	54	80	7	4	9
Narcotics	41	44	12	10	34
Barbiturates	25	20	16	12	57
Analgesics	185	16	19	12	53
Gastrointestinal	25	16	8	24	52
Bromides	25	8	20	4	68
Endocrines	15	7	0	7	86
Patent nostrums	29	4	14	10	72

various periods, ranging from a single trial to the prolonged use of a drug for more than fifty doses. The therapeutic results, as reported by the patients, are summarized in Table 1.

The group of vasoconstrictors included the cerebral vasoconstrictor, caffeine,³ and the dural vasoconstrictor, ergotamine.⁴ Both seemed to be highly effective, although the small number of patients who had tried caffeine (6 cases) precludes an

*From the Neurological Unit, Boston City Hospital, and the Department of Neurology, Harvard Medical School.

†Clinical psychologist, Waulington an Hospital.

‡Formerly assistant visiting neurologist, Boston City Hospital and instructor in neurology, Harvard Medical School.

§Associate in psychiatry, Harvard Medical School and assistant visiting psychiatrist, Boston City Hospital (on leave of absence).

adequate evaluation of this alkaloid. Eighty per cent of those using ergotamine reported complete relief from the migraine attacks. Because some used the drug orally and others by hypodermic, the percentage relieved is a composite of the relief obtained by the less effective oral and highly effective parenteral routes.⁵

The narcotic group consisted of morphine, pantopon, codeine and scopolamine. Morphine and codeine were most effective, the former being reported to be completely effective in 59 per cent of the patients who used it. However, relief was conditional on the ability of the narcotic to cause sleep or to depress the patient's general physiologic state.

The barbiturates included phenobarbital, Pentobarbital and Allonal. Phenobarbital helped 16 per cent of the patients who tried it.

Under analgesics were classified such drugs as acetanilid, acetylsalicylic acid, amidopyrine, phenacetin and various proprietary remedies containing these substances. Acetylsalicylic acid was successful in giving relief to 10 per cent of the 186 patients assumed to have tested it adequately.

Among the drugs acting on the gastrointestinal system were dilute hydrochloric acid, sodium bicarbonate, Seidlitz powders and various proprietary preparations; Seidlitz powders were the most effective of this group, 18 per cent of its users reporting it helpful. These remedies did not seem to act directly on the headache, but rather relieved the distress due to nausea and vomiting, so that their value in alleviating discomfort from migraine is secondary if not open to question.

Of the bromides, including Bromo-Seltzer and the various bromide salts, Bromo-Seltzer was slightly more helpful than the other drug preparations, but as a whole this group may be said to be relatively ineffective in migraine therapy.

Although not many patients in this study were treated with endocrine substances, the results are included as evidence concerning the casual use of endocrines for migraine. Thyroid, Theelin, Progynon, Hormatone and anterior pituitary extract were administered. Only 1 patient was satisfied with the relief obtained. This patient received pituitary extract. Obviously, these observations are not sufficient to warrant any comment other than that they reflect the results usually obtained from casual application of endocrines in office practice.

Because of the widespread advertising of proprietary medicines described as "headache remedies," it is remarkable how few migraine sufferers have tested them. Of the 29 who did, only 4 per cent obtained adequate relief.

In addition to the cases analyzed above, various drugs acting on the autonomic nervous system were used without success. Seven patients used vasodilators, but none were adequately relieved. Laxatives were reported as fairly helpful by 4 of the 7 patients trying them.

SUMMARY

It may be said that many misinterpretations are made in the evaluation of headache remedies, especially in the therapy of migraine. In this study, there was considerable difficulty with some of the patients in determining whether the particular headache treated by a given drug was actually migrainous, although the patient suffered from migraine attacks at certain times. Side actions of the various drugs may have afforded some secondary relief without affecting the headache itself.

The greatest relief was from drugs in the vasoconstrictor group, consisting mainly of favorable reports on the use of ergotamine tartrate by 80 per cent of its users, in spite of the unpleasant and pronounced side actions. This re-emphasizes the observation that drugs causing vasoconstriction of the branches of the external carotid artery⁶ are by far the most successful in terminating or aborting migraine headaches. Analgesics were tested most frequently by the greatest number of cases, but with comparatively unsatisfactory results.

Perhaps newer therapeutic methods, such as oxygen inhalation,⁷ vitamin B₁ therapy⁸ and arterial ligation⁹ will prove effective in the future. Until such time, ergotamine tartrate remains the most effective means of terminating a migraine attack.

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INTRINSIC DISEASES OF THE LIVER SIMULATING ACUTE CHOLECYSTITIS

FIRST LIEUTENANT KNOWLES B LAWRENCE, MC, AUS,* AND HOWARD M CLUTE, M.D†

BOSTON

IN RECENT years many surgeons have accepted the principle of early operation as the safest method of handling acute cholecystitis. This means that surgery in many such cases will be done as soon as the patient's condition permits and before time has allowed elaborate laboratory studies. It is frequently necessary, therefore, to differentiate clinically between acute cholecystitis and certain other upper abdominal conditions that may be more suitably handled by conservative means. Our recent experience shows that certain intrinsic diseases of the liver may simulate acute cholecystitis so closely that clinical differentiation is difficult, if not impossible.

The pathologic changes in acute cholecystitis in the early period—that is, the first twenty-four to seventy-two hours after onset—are essentially mechanical in character, as has been demonstrated by a number of investigators at this clinic¹ and elsewhere.^{2,3} The process starts with the blocking of the cystic duct, usually by an impacted gall stone. The resulting edema and venous stasis in the wall of the cystic duct plus obstruction to the outflow of gall bladder contents set up a vicious circle resulting in a high degree of vascular and lymphatic block of the entire gall bladder. Local ischemic necrosis of the gall bladder wall may then take place, with perforation resulting if the area involved is large enough.

Changes such as these should, and usually do, produce a fairly standard clinical picture. Initially there is local colicky pain, acute or subacute in onset, as the gall bladder attempts to force an impacted stone through its too narrow cystic duct. Pain of such origin commonly radiates also around the right lower costal margin to the right scapular region. Nausea and reflex vomiting may occur in this stage. As the circulatory changes progress the gall bladder becomes distended, its musculature is less able to contract, so that the colicky pain is superseded by an intense dull ache, a visceral pain due to overstretching of the peritoneal coat. The viscus may then be palpable as a tense and very tender mass below the right liver margin. This is the stage in which the patient is often seen by the surgeon, it may occur a few hours to a few days after onset. Despite the usual absence of

bacterial inflammation, there is characteristically a slight rise in temperature and pulse rate and a moderate polymorphonuclear leukocytosis. Later in inflammatory reaction of the serosa may be manifested by tenderness and muscle spasm over the gall bladder region. Perforation of the gall bladder with peritonitis is usually obvious to the examiner as an acute surgical emergency.

Thus, when one considers acute cholecystitis in the light of the pathologic process, it becomes apparent that certain diseases of its neighbor, the liver, might well simulate its clinical picture. The following morbid mechanisms might be postulated: necrosis in a tumor nodule growing more rapidly than its blood supply, thus causing a considerable reaction on the peritoneal surface, stretching of Glisson's capsule by an underlying hemangioma, abscess or echinococcus cyst of the liver, and a more diffuse hepatic inflammation causing pain through both the above mechanisms plus possible affection of the visceral sensorium—for example, a fulminating acute hepatitis or yellow atrophy. Fever, leukocytosis, systemic debility or reflex gastrointestinal symptoms may be as commonly associated with certain of these conditions as with acute cholecystitis.

At the Massachusetts Memorial Hospitals we have encountered several cases of intrinsic liver disease which simulated acute cholecystitis so closely that the diagnosis was often difficult and uncertain. These cases, with comments on their diagnosis and management, are as follows:

CASE 1. A 56-year-old white woman entered the hospital complaining of right upper-quadrant pain of 5 days duration. Fifteen years and 2 years previously she had had attacks of pain and indigestion and x-ray films were said to have shown trouble with the gall bladder. Similar symptoms set in 6 weeks before admission. She had had some vomiting also and diarrhea without blood. Five days before admission severe right upper-quadrant pain began with radiation to the right posterior shoulder region, mild chills and fever. There was a 34 pound weight loss in 3 months.

On examination the patient appeared in acute pain. A tense, rounded, very tender mass, the size of a small fist, was felt in the gall bladder region. The liver edge could be palpated 5 cm. below the right costal margin, rounded and slightly tender. On rectal examination a hard polypoid mass involving the anterior rectal wall and invading the pararectal tissues, an obviously malignant neoplasm, was found. The admission temperature was 102.4°F, the pulse 100, and the white-cell count 15,000, with 84 per cent polymorphonuclears.

Laparotomy was performed shortly after admission, and the mass felt preoperatively was found to be a hard tumor

*Assistant in surgery, Boston University School of Medicine, and assistant surgeon, Massachusetts Memorial Hospital (on leave of absence).

†Professor of surgery, Boston University School of Medicine, surgeon-in-charge of Massachusetts Memorial Hospital.

nodule imbedded in the liver. Just medial to it lay the virtually normal gall bladder. There were multiple tumor nodules throughout the liver, and a biopsy of one of these showed an anaplastic, rapidly growing metastatic adenocarcinoma. The patient died 6 weeks later.

The clinical picture in this case so closely simulated that of acute cholecystitis that early operation seemed the wiser course, despite the knowledge preoperatively of the patient's carcinoma of the rectum. Had the routine rectal examination been omitted, as it is at times, unfortunately, the case for acute cholecystitis would have been even stronger. We surmise that the symptoms and signs in this case were due to necrosis within the large tumor nodule lying just to the right of the gall bladder.

CASE 2. A 67-year-old white man, a physician, was admitted because of bowel symptoms and weight loss. Five years previously a resection of 12 cm. of transverse colon had been performed for a "malignant polyp" at another hospital.

The physical examination was essentially negative. The patient was studied in great detail without definite findings. Three weeks after admission he developed rather suddenly a severe right-upper-quadrant pain with tenderness and spasm in the right subcostal region. The liver edge was palpable and possibly somewhat irregular. The temperature was 99.6°F. and the white-cell count 11,300, with 87 per cent polymorphonuclears.

A previous cholecystogram had demonstrated a probable chronic cholecystitis and cholesterosis. No stones were seen. In view of the clinical picture at this time a diagnosis of acute cholecystitis was considered, but the probability that the symptoms were due to metastatic liver disease was so strong that operation seemed unwarranted. The symptoms subsided somewhat, and the patient died several weeks later of general carcinomatosis, including the liver, and terminal pneumonia.

CASE 3. F. B., an 83-year-old white man, was admitted to the Massachusetts Memorial Hospitals on April 16, 1942, complaining of severe right-sided abdominal pain for 4½ days' duration. At first this pain was felt in the right midabdomen, then 24 hours later worked up into the right upper quadrant and beneath the costal margin, where it persisted as a fairly constant, severe aching pain. The pain did not radiate, but was severer when the patient breathed deeply or moved about.

During the previous year the patient had become increasingly constipated and had experienced frequent bouts of painless vomiting lasting a day or more, usually occurring when he was constipated. There was no pain associated with this. He had been passing gas satisfactorily up to the time of admission. There was no history of chest pain. The patient's health prior to this trouble had been reasonably good for his age. He had had a suprapubic prostatectomy for benign prostatic hypertrophy 3 years previously.

Examination showed an emaciated elderly man in obvious pain lying on his left side with the legs drawn up. The rectal temperature was 101°F., the pulse 92, and the blood pressure 118/80. Marked generalized arteriosclerosis was noted. The heart and lungs were normal for the patient's age. The abdomen was slightly distended and was resonant throughout. It was generally soft ex-

cept for definite spasm of the right-upper-quadrant muscles near the costal margin and definite tenderness over this same area. A poorly defined mass, possibly 6 cm. in diameter, could be felt and percussed in this area and seemed to come from beneath the costal margin. Peristalsis was somewhat hyperactive throughout the abdomen.

The white-cell count was 10,200, with 78 per cent polymorphonuclears, and the red-cell count 3,190,000, with a hemoglobin of 64 per cent. The nonprotein nitrogen was 43 mg. per 100 cc., and the icteric index 10. Urinalysis revealed a trace of albumin, many white cells and rare red cells. The urinary diastase was less than 4 units. A flat x-ray film of the abdomen showed no opaque calculi. The colon appeared distended with gas. A barium enema done the following day showed a diverticulosis and a diverticulitis of the sigmoid and colon without obstruction.

A provisional diagnosis of acute cholecystitis was made. It was thought that the process was localized and would probably subside with conservative treatment. In view of this and the patient's extreme age, operation was deferred.

The patient was given sulfadiazine by vein and by mouth and a sufficient quantity of intravenous fluids. He continued to run a low-grade septic course with the temperature ranging between 99.6 and 102°F. (rectal). The white-cell count varied between 11,000 and 17,000. The pain and tenderness persisted. The right-upper-quadrant mass became larger and considerable fluid accumulated in the abdomen. The patient was thought to have developed a pericholecystic abscess.

Operation was therefore performed, with intent to drain the gall bladder, 8 days after admission. The finding, however, was an enlargement of the liver by irregular infiltrations with yellow tumor tissue. The biopsy diagnosis was primary hepatoma. The gall bladder was not inflamed. The patient went downhill rapidly and died 36 hours later.

Autopsy revealed massive enlargement of the liver by primary hepatoma, which in two places had grown into the stomach wall. The gall bladder showed no disease.

This case closely resembled one due to acute cholecystitis. Even in retrospect, no direct clinical leads to the correct diagnosis are apparent.

CASE 4. A 36-year-old Negro entered the hospital complaining of severe retching, vomiting and malaise of 3½ days' duration. He denied real pain—only a slight upper-abdominal soreness. The vomitus was reflex rather than obstructive in type, and the patient's evacuations continued fairly normally. He dated his illness from the inhalation of fumes from an accidentally broken fire-extinguisher bulb containing carbon tetrachloride. Eighteen months before entry, on a previous admission for gonorrheal epididymitis, the liver edge had been felt three fingerbreadths below the costal margin; the patient was given 40 gr. of sulfanilamide daily for 6 days for his gonorrheal infection. He was known to have been a chronic alcoholic for several years. There was no history of definite gastrointestinal symptoms prior to the present illness.

On examination the temperature was 102°F., and the pulse 100. The patient was acutely ill, groaning with pain and rolling from side to side with the thighs flexed on the abdomen. The upper two thirds of the abdomen, particularly on the right side, was nearly boardlike and exquisitely tender. This splinting, plus a well-developed musculature, prevented satisfactory palpation or even percussion of the upper abdomen. The liver margin could

not be palpated. Jaundice was not apparent, as the patient was a Negro and was seen after nightfall. The white-cell count was 31,000. The urine contained a trace of bile. X-ray films of the abdomen and diaphragmatic area showed the liver somewhat enlarged, but no free gas or other abnormalities. Despite an atypical history, it was believed that the signs were those of an acute upper abdominal peritonitis possibly from a perforated gall bladder or peptic ulcer, and that immediate operation was imperative.

On opening the abdomen an acute hepatitis with free bile stained peritoneal fluid and toxic regional lymphadenitis was found. A biopsy specimen from the liver was diagnosed acute hepatic necrosis (central type). Following the operation the patient declined rapidly and died 1½ days later. An autopsy revealed a hemorrhagic central necrosis of the liver, probably due to carbon tetrachloride poisoning, toxic nephrosis and pulmonary edema.

This case illustrates the well known fact that certain cases of acute hepatitis present a clinical picture difficult to differentiate from acute surgical conditions of the upper abdomen. Knowledge of this combined with the history of exposure to a hepatotoxic drug should make the surgeon doubly wary.

In studying the literature, we were able to find little on the subject of diseases of the liver simulating acute cholecystitis. However, the following conditions, which at times have produced similar clinical pictures, are mentioned, ruptured hemangioma, spontaneous rupture of the liver and

spontaneous subglissonian hemorrhage, simple cysts of the liver with or without rupture, tuberculoma and gumma, echinococcal cyst, amebic abscess, pyogenic abscess and neoplasms of the liver, primary or metastatic.

CONCLUSIONS

Acute hepatic disease may simulate acute cholecystitis as to sudden onset, low fever, an elevated white cell count and a tender mass in the right upper quadrant.

A history of exposure to a hepatotoxic drug should lead one to consider the possibility of acute yellow atrophy.

The clinical picture of acute cholecystitis may also be simulated by primary or metastatic cancer of the liver, particularly when secondary hemorrhage or necrosis has occurred. A history of previous malignancy should make one suspicious of this.

These and other intrinsic diseases of the liver are occasionally difficult to differentiate from acute cholecystitis.

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PRIMARY CARCINOMA OF THE APPENDIX ASSOCIATED WITH ACUTE APPENDICITIS

Report of a Case

EDWARD L. YOUNG, M.D.,* AND FIRST LIEUTENANT STANLEY WYMAN, M.C., A.U.S.

BOSTON

PRIIMARY carcinoma of the appendix must be differentiated from carcinoid of the appendix and carcinoma of the cecum. Failure to distinguish between these conditions has led to an unfortunate confusion in the literature.

Carcinoid is a disease usually found unexpectedly by the pathologist. Eighty-two per cent of cases occur in females,¹ and the greatest incidence is found in the third decade.² Such cases comprise less than 0.4 per cent of all intestinal cancers.³ Carcinoids are usually firm ovoid tumors, often yellow, located near the tip of the appendix. They are composed of cells originating from the Kulchitzky cells in the bases of Lieberkuhn's glands. Because the cells contain silver reducing granules,

the tumors are often called argentaffinomas. They resemble basal cell epitheliomas in that they often form sheets or islands of cells with occasional mitoses. In general, they act as benign tumors, but metastasize to the liver and regional lymph nodes have been reported.

Carcinoma of the cecum most frequently takes the form of a large fungating mass that may occlude the lumen of the appendix or infiltrate its base, at times giving rise to symptoms of appendiceal obstruction. Many cases of carcinoma of the cecum are reported in the literature, in contrast to primary carcinoma of the appendix.

True carcinoma of the appendix is primary in that organ and is usually colloid in type.⁴ It causes no specific signs or symptoms, but at times the patient may give an atypical history of appendicitis or may have recurrent attacks of right lower

*Surgeon chief, Faulkner Hospital, vs. surg. colon, Massachusetts General Hospital.

†Formerly, house officer, Faulkner Hospital.

quadrant pain. It may make itself known as a mass in the abdomen, cause a generalized peritonitis by perforating the bowel or obstruct the lumen of the appendix. The literature of the last ten years contains many reports of carcinoma of the appendix, but close examination reveals only 4 cases of apparently true primary carcinoma—Darnall and Kilduffe,⁵ Blumenkopf,⁶ Heine⁷ and Frauenthal and Grausman.⁸

CASE REPORT

A 36-year-old married man entered the Faulkner Hospital on June 24, 1940, complaining of pain in the abdomen. Two weeks before entry, he had an episode of pain in the abdomen preceded by soreness low in the back. Abdominal pain lasted 4 or 5 days and was accompanied by fever, but there was no nausea or vomiting. A physician told the patient that he had mild appendicitis and that if he had a recurrence he should be operated on. On the day before entry, the patient noticed slight twinges of pain in the right lower abdomen, but he went to bed and slept well. He awoke with a sensation of soreness in the lower abdomen. During the course of 2 hours, the pain increased rapidly in severity, and by 11 a.m. the patient was almost doubled up with crampy abdominal pain. There was no nausea or vomiting, and the bowels moved normally on the day of entry. There was no pain or burning on urination, and no hematuria, pyuria, recent cold or pain in the chest. The past and family histories were irrelevant.

Physical examination revealed a well-developed and well-nourished man lying in bed with the legs bent. The height was 5 feet, 8 inches, and the weight 200 pounds. The temperature was 101°F., the pulse 74, and the respirations 20. The tongue was coated, and the throat slightly injected. The heart and lungs were normal. There was no costovertebral tenderness. The abdomen was flat, and no organs or masses were palpable; there were no hernias. Slight spasm was apparent in the right lower quadrant, with very definite acute tenderness in a sharply localized area over McBurney's point. Pain and rebound tenderness followed pressing in the left lower quadrant. Rectal examination was negative. The reflexes were physiologic.

Laboratory studies showed a white-cell count of 10,500 with 79 per cent polymorphonuclear leukocytes. Examination of the urine was negative. A flat plate of the abdomen was negative for localizing signs and for kidney stones.

A diagnosis of acute appendicitis was made. Under spinal anesthesia, a right pararectus incision was made. When the abdomen was opened, some cloudy fluid was present, and the appendix was found to be greatly swollen and stiff, with one gangrenous area. The base was edematous and porky in consistence. The appendix was excised at its base, the stump buried, and the abdomen closed in layers without drainage. At this time, there was no suspicion that cancer was present.

Pathological examination showed an appendix measuring 6 cm. in length and 1.5 cm. in diameter. The surface varied from red to pink and showed occasional patches of yellowish fibrin. The wall was moderately distended, and at a point 2 cm. from the tip, there was a constricted area. The lumen was found with difficulty, especially in the proximal portion. The wall was markedly thickened, the cut surface being glistening and white. The distal half of the appendix showed a fairly definite lumen filled

with grayish fluid and a few smooth, hard, black masses measuring up to 0.3 cm. in diameter. When the larger masses were cracked, they were found to contain seeds.

Microscopically, three sections showed infiltration of the wall by small islands of cells, which frequently occurred as signet cells and were surrounded in part by bluish-staining mucoid material. In two sections, a rather broad area in the mucosa, although not extending entirely through the surface, presented an increase in connective tissue through which were scattered individual signet cells and small cords of cells. An occasional luminated structure was found, and frequent mitoses were present. In addition, the mucosa showed patches of necrosis, and the lumen contained polymorphonuclear leukocytes in several sections. On the outer surface, there was a mass of fibrinopurulent exudate, and, in one region, large numbers of bacteria, occurring as an abscess in the periappendiceal fat tissue. Figure 1 shows the histologic picture of the

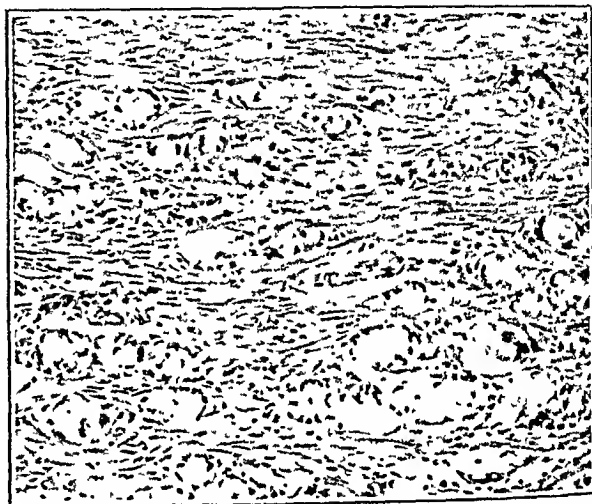


FIGURE 1. High-Power View of a Section of the Tumor.

tumor. Diagnosis: primary carcinoma of the appendix, occurring chiefly as the colloid type, and acute appendicitis, with abscess formation and masses of bacteria on the serosal surface.

Three weeks later, an ileotransverse colostomy was performed. The germinal ileum for a distance of 60 cm. was found adherent to the cecum. In addition, there was a Meckel's diverticulum 45 cm. from the cecum. The patient made an uneventful recovery from this operation, and 10 days later, a right colectomy was done, the terminal 45 cm. of ileum, the cecum, ascending colon and hepatic flexure being removed. Histologic examination showed a few small islands of colloid carcinoma in the outer portion of the muscularis at the site of the appendiceal stump, but none elsewhere; the regional lymph nodes showed chronic inflammation but no evidence of tumor.

At a follow-up examination more than two years following the last operation, the patient stated that he had been symptom free and had been doing hard physical labor; neither x-ray nor physical examination revealed evidence of recurrence.

SUMMARY AND CONCLUSIONS

The literature for the past ten years is reviewed, true carcinoma confined to the appendix being found to be quite rare.

A case of acute appendicitis complicated by colloid carcinoma is reported

Colloid carcinoma of the appendix may cause no specific symptoms or signs, and since carcinoma may be indistinguishable grossly from acute inflammation, microscopic examination of all appendices removed at operation should be done

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MEDICAL PROGRESS

THE BILE PIGMENTS (concluded)[†]

CECIL JAMES WATSON, MD †

MINNEAPOLIS

Recent clinical advances In 1936, a further modification of Terwen's method for the quantitative determination of urobilinogen in urine and feces was described.⁷¹ It was shown that the color intensities of mesobilirubinogen aldehyde and stercobilinogen aldehyde, as developed with Ehrlich's reagent in this method, were identical. More recently, this has been confirmed by means of the Evelyn photoelectric colorimeter, and the method has been applied to it,⁷² with excellent results.

Studies of jaundice, with particular reference to the daily excretion of urobilinogen in the feces and urine,⁷²⁻⁷⁵ have shown that helpful fundamental and diagnostic information may often be gained. With a modification of Rich's⁷⁴ classification of jaundice, as given below, the various forms noted are characterized in the main by urobilinogen excretion as indicated. The normal range was found to be 40 to 280 mg per day for the FU (feces urobilinogen)—usually 100 to 200 mg—and 0 to 35 mg per day for the UU (urine urobilinogen)—most frequently 0.5 to 1.5 mg. The value for the feces is an average for a four day period, whereas that for the urine is for 24 hours.⁷¹⁻⁷³⁻⁷⁵

I Retention jaundice may be defined as hepatocellular inability to remove bilirubin from the circulating blood, with resultant accumulation. There is an indirect or delayed van den Bergh reaction and no bilirubinuria.

A Hemolytic jaundice may be spheroidocytic or macrocytic, and the former may be familial or acquired in type. The FU ranges from 300 to 4000 mg per day, usually 600 to 2000 mg, and the UU varies from 10 to 200 mg per day, usually 50 to 300 mg.

The feces urobilinogen is commonly higher in patients with marked anemia or with hemolytic crises, but there is not a strict correlation.⁷⁶ Cases are seen with high values but relatively little anemia.⁷⁰ Contrary to frequently expressed belief, cases are often encountered with a marked increase in feces urobilinogen, but with a normal amount in the urine.⁷⁰ Such patients may have marked anemia, but relatively little, or even no, jaundice.⁷⁻⁷⁰ In general, it may be stated that the more anemia, the less jaundice and urobilinogenuria and vice versa. The immediate period of hemolytic crises constitutes an exception to this, however.

B Constitutional hepatic dysfunction consists in constitutional hepatocellular inferiority in bilirubin excretion into the bile. This condition may or may not be familial. It has been described under various names and by different investigators,^{1,7-70} more recently by Dameshek,⁸⁰ under the designation of "familial nonhemolytic jaundice." The abnormality is characterized by simple accumulation of bilirubin, there is neither splenomegaly, spheroidocytosis or reticulocytosis nor any evidence of hepatic functional impairment other than faulty excretion of bilirubin.

The FU ranges from 100 to 200 mg, and the UU from 0.5 to 3.5 mg per day.

C Various factors, such as chronic passive congestion (often with pulmonary infarcts),

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[†]From the Division of Internal Medicine, University of Minnesota Hospitals.

[†]Professor of Medicine, University of Minnesota, Chief of Medical Service, University of Minnesota Hospital.

Watson C. J. Unpublished data.

pneumonia, virus and other infections, and poisons like arsphenamine and sulfanilamide, may produce a *mild retention jaundice*. This may become more marked, with developing evidence of regurgitation jaundice, or it may recede without this. Pure retention jaundice may be noted in the convalescent or later stages of any type of hepatitis. Not infrequently, especially with jaundice due to heart failure or pneumonia, a mild hemolytic component is present, as reflected in an elevated feces urobilinogen. The urine urobilinogen is nearly always elevated.

The F.U. varies from 100 to 500 mg. per day, usually 200 to 300 mg., and the U.U. from 5 to 100 mg. per day, usually 10 to 30 mg.

II. *Regurgitation jaundice* is caused by leakage or regurgitation of bile into the blood. Depending on the factors given below, this is due either to increased intrabiliary pressure with actual "rhexis" of the bile capillaries (especially ampullas) or smaller ducts,⁸¹ or to damage of these structures, resulting in increased permeability.^{82, 83} In either event, the bile probably gains access first to the lymph spaces of Desse, thence to the thoracic duct and the blood.^{81, 82, 84} The van den Bergh reaction is prompt or biphasic and bilirubinuria is present.

A. The *mechanical type* is caused by regurgitation of bile due to increased intrabiliary pressure.

1. *Cancer of the biliary tract* includes carcinoma, either primary or metastatic, and tumors of the lymphoblastoma group. The term "biliary tract" refers to the main hepatic ducts, the common hepatic duct, the common bile duct or the ampulla of Vater. Cancer involving these structures may be primary or secondary. A smooth, nontender, distended gall bladder is often palpable. There is complete biliary obstruction in about 90 per cent of cases.

The F.U. is less than 5 mg., and the U.U. less than 0.5 mg. per day.

Incomplete biliary obstruction is encountered in less than 10 per cent of cases.⁸⁵ This group includes polypoid and necrotic tumors and minute ampullary or common-duct carcinomas.^{73, 75} It may be emphasized that the depth of jaundice is not determined solely by the degree of biliary obstruction. Decreased bilirubin formation, or "throttling" of blood destruction following blood loss, results in a decrease of jaundice even though the biliary obstruction may remain complete.^{85, 86}

2. With *calculi*, the jaundice is usually fluctuant or intermittent. Colic and chills are com-

monly noted. Incomplete biliary obstruction is present in approximately 90 per cent of cases.⁸⁵

The F.U. ranges from 7.0 to 600 mg., and the U.U. from 0 to 50 mg. per day. This variation depends on several factors. With rapidly diminishing jaundice after spontaneous release of the obstruction, large amounts may be encountered for a short period. With low-grade obstruction, the amount may be within the normal range, although in some cases of this type it may be markedly decreased, probably because of a diminished rate of blood destruction. An impacted stone might be expected in a case with complete biliary obstruction. In my experience, this has usually not been found. Several cases have been observed in which the stone or stones were entirely loose in the duct and in which the reason for the complete obstruction was not apparent⁸⁵; conversely, impacted stones have been noted in several cases with incomplete obstruction.⁷³

The amount of urobilinogen in the urine depends on several factors, among which may be mentioned: the duration of the biliary obstruction and whether biliary or obstructive cirrhosis has developed; the presence or absence of cholangitis; and the degree of obstruction. Small amounts of urinary urobilinogen indicate hepatic functional impairment if but small amounts are present in the feces. This is probably true in jaundice of whatever cause.⁷³

3. In the majority of cases of *postoperative or benign stricture*, the obstruction is incomplete, but it appears that complete obstruction is encountered more frequently than with a common-duct stone.⁸⁵

The F.U. ranges from 0 to 300 mg., and the U.U. from 0 to 50 mg. per day. This variation of urobilinogen depends on the factors discussed in the foregoing paragraph.

4. *Chronic pancreatitis* causes jaundice but rarely; data on urobilinogen excretion are available from only 2 cases.⁸⁵ In one of these, the icterus was mild, and the biliary obstruction was not high grade; in the other, the clinical picture was that of carcinoma of the head of the pancreas, with the exception that the feces contained 9 to 22 mg. of urobilinogen per day during two four-day collections. The amount in the urine was negligible. This patient presented an easily palpable, nontender, distended gall bladder. At operation, the surgeon thought he was dealing with a carcinoma of the pancreas and performed a cholecystgastrostomy. The patient died of a postoperative hemorrhage (vitamin K at that time had not become available). Histologic

study of the pancreas obtained at autopsy first clarified the diagnosis, revealing a diffuse chronic fibrous pancreatitis.

B. The *parenchymal type* is any regurgitation jaundice due to diffuse liver damage (not secondary to mechanical obstruction). Acute and chronic hepatitis, damage due to toxins and chemicals, cirrhosis, diffuse carcinomatosis, and chronic passive congestion are included. Regurgitation of the bile is mainly the result of increased permeability of the bile capillaries (ampullas and small bile ducts and, at least in some cases, of intrahepatic bile-duct or bile-capillary obstruction, because of swelling of the liver cords, edema of the spaces of Disse³⁰ or fibrosis in the portal areas of the liver lobules.

The F.U. varies from 0 to 1000 mg. per day, usually 10-300 mg., and the U.U. from 0 to 300 mg., usually 0.5 to 100 mg. Of 57 cases of various types of parenchymal jaundice, only 2 (3.5 per cent) exhibited less than 5 mg. of fecal urobilinogen per day. Six were found to have less than 1 mg., and 4 less than 0.3 mg. in the twenty-four-hour urines.⁸⁵ These values may be compared with those given above for biliary-tract cancer and the calculous group.

1. *Hepatitis* may be divided into the groups shown in Table 1, with their corresponding

TABLE 1. *Types of Hepatitis with Particular Reference to Urobilinogen Excretion.*

Type	UROBILINOGEN EXCRETION	
	F.U. mg./day	U.U. mg./day
Acute		
Early period (2 to 4 days)	10-100	10-100
Peak of jaundice (4 to 8 days)	0-20	0-10
Diminishing jaundice (7 to 30 days)	50-600	10-300
Subacute (1 to 2 months)	10-1200	0.5-300
Subchronic (2 to 6 months)	10-1200	0.5-300
Chronic (cirrhosis)		
With marked jaundice	10-1200	0.5-300
With mild or no jaundice	50-300	0.5-30

ranges of urobilinogen excretion. It is seen that, in some cases of acute hepatitis, urobilinogen is absent from the urine and feces during the peak of the jaundice. Insufficient data are available regarding the actual percentage of cases with complete exclusion of bile from the intestines during the height of the disease. The majority of cases that have been studied were first seen when the jaundice had already been present for some time and was beginning to diminish. From the available evidence, there is little doubt that a temporary, complete exclusion is not uncommon. Judged by simple inspection or by quali-

tative tests alone, however, complete exclusion has undoubtedly been believed to be commoner than it is. Grossly acholic feces may contain from 10 to 15 mg. of urobilinogen per day; correspondingly, a twenty-four-hour-urine sample may exhibit a negative qualitative Ehrlich reaction, and yet by the quantitative method^{73, 75} as much as 15 mg. per day may be detected. During the third or receding stage of acute hepatitis, urobilinogen usually reappears in the urine in large amounts. Serial qualitative tests are of much value at this point, since they often reveal the first evidence of beginning improvement—that is, the re-establishment of bile flow to the intestine. From this point on, the progress of convalescence may be followed by observation of the urobilinogen reaction each day. In a small percentage of cases of acute catarrhal jaundice, urobilinogenuria fails to appear during the convalescent period. It remains to be determined whether these are examples of catarrhal jaundice in the true sense of the word—a “catarrhal choledochitis”⁸⁷—or whether an actual hepatitis.

As noted above, a considerably increased fecal urobilinogen excretion may be observed as the jaundice diminishes in acute hepatitis and also, for longer periods and in greater degree, in the more prolonged cases, including some of those that progress to cirrhosis. There is every reason to believe that these increases are often associated with an increased rate of blood destruction. Outspoken hemolytic anemia may develop, with macrocytosis and increased reticulocytes.^{73, 76, 78} Splenic enlargement is usually marked. In van den Bergh and Kamerling's⁸⁸ fatal case of this type, there was a large amount of hematin in the circulating plasma. In passing, it might be noted that hematinemia has been emphasized repeatedly as an evidence of liver damage. Whether this is actually hematin or Fairley's⁸⁹ methemalbumin has not been determined.

2. *Toxins*, such as those occurring in pneumonia, peritonitis, hemolytic-streptococcus septicemia, gas-bacillus sepsis and other severe toxemias, may produce liver damage. F.U. ranges from 100 to 400 mg., and the U.U. from 10 to 200 mg. per day.

3. *Poisons*, such as arsphenamine, cinchophen, phosphorus, trinitrotoluene, sulfanilamide and many other substances, may result in liver damage. The F.U. varies from 10 to 1000 mg., and the U.U. from 0.5 to 300 mg. per day.

The jaundice seen following arsphenamine or cinchophen may be associated with almost complete suppression of bile flow—in some cases, quite complete. Arsphenamine jaundice may

simulate acute or subacute hepatitis, or so-called "catarrhal jaundice" quite closely. On the basis of clinical and histologic studies (liver biopsy) in 10 cases, Roholm and Krarup⁹⁰ have recently stated that arsphenamine simply lowers the resistance of the liver to the virus of epidemic hepatitis. Hanger and Gutman⁹¹ have described cases of arsphenamine jaundice similar to what Eppinger calls the "cholangiolitic type" of catarrhal jaundice in distinction to the ordinary, hepatocellular variety. Although there is no doubt of the existence of the two clinical types, there are many borderline cases, and so far as can be determined at present, there are no disturbances of pigment metabolism that are distinctive.

Cinchophen jaundice may likewise simulate acute hepatitis, especially in the appearance of the pigments. In a case previously recorded,⁷³ there was a history of recent ingestion of pills (probably cinchophen) for "rheumatism." Painless, deep jaundice, with anorexia and nausea, developed. At the height of the jaundice, the F.U. was 10.2 mg., and the U.U. 3.8 mg. When the jaundice had diminished, the former was 280 mg., and the latter 207 mg. This case illustrates well the high-grade but incomplete biliary obstruction, the importance of evaluating a relative increase of urobilinogen in the urine in favor of liver damage and, finally, the large amount in the urine during the re-establishment of bile flow, owing to residual disturbance of liver function.

Jaundice following sulfanilamide is rarely intense or associated with a very marked suppression of bile flow. There may be a prominent hemolytic factor, with outspoken anemia and increased fecal urobilinogen.⁹² Occasionally, cases are seen in which the jaundice deepens rapidly and death is due at least in part to severe hepatic injury, even acute atrophy. In my experience, however, jaundice of this degree has been observed only when there was reason to believe that the liver was damaged before the administration of sulfanilamide—for example, in the presence of severe infections or toxemias or when the drug was given to a patient also receiving arsphenamine treatment for syphilis.

4. Cirrhosis of the liver is of various types. In the foregoing discussion of "hepatitis," the chronic form was noted as being synonymous with cirrhosis. This does not indicate that all types of cirrhosis follow hepatitis. On the contrary, many are probably related to other factors, of which fatty liver, deficiency states (including chronic alcoholism) and various poisons, notably cinchophen and arsphenamine, may be emphasized. From the standpoint of the bile pigments, however, no fea-

tures differentiate the various etiologic factors. This is also true of hemochromatosis, although it may be noted that jaundice is usually not prominent in this disease.

5. In some cases of *diffuse carcinomatosis*, hepatic metastases are sufficiently extensive to impair liver function markedly. Considerable jaundice may be noted, even though the main hepatic ducts are uninvolved. Marked urobilinogenuria may occur,⁸⁵ and the clinical picture may closely simulate cirrhosis of the liver.

6. *Chronic passive congestion* has already been referred to as a cause of retention jaundice. In severe cases of so-called "cardiac jaundice," regurgitation jaundice is nearly always present as well.⁹³ Pulmonary infarcts are commonly found.⁹⁴ Urobilinogenuria is usually noted, and is often marked. Edelman and his co-workers⁹⁴ found an excess of urobilin in 88 per cent of their cases of heart failure. The presence of renal insufficiency or azotemia usually prevents or reduces urobilinogenuria.⁹⁵ Correspondingly, when crystalline stercobilin is administered intravenously in a patient with both hepatic and renal impairment, its elimination in the urine is markedly retarded.¹

Pulmonary or myocardial infarction is often productive of marked urobilinogenuria. Head⁴ has shown that serial qualitative urine urobilinogen tests are helpful in the diagnosis and care of coronary thrombosis and its complications. There is considerable reason to believe that this indicates liver damage due to substances coming from the infarct. Urobilinogenuria occurring after a ruptured tubal pregnancy has been similarly explained.⁹⁶ After an attack of coronary thrombosis productive of an infarct, the urobilinogen reaction rarely becomes positive before the end of the first twenty-four hours and usually not before two or three days, quite in contrast with an acute biliary colic or acute cholecystitis, in which the reaction often appears almost at once. In the latter condition the urobilinogenuria is believed to be due to lymphatic drainage of bacteria or toxic material from the gall bladder into the liver, with resultant hepatitis or liver-function impairment.⁷³

The simple qualitative test for urobilinogen⁷¹ often yields valuable information, although it is true that in many cases nothing very decisive can be found without quantitative determination of the per-diem amounts in the feces and urine. Positive reactions in the feces usually indicate patency of the biliary tract, or at least that biliary obstruction

*Head, D. P. Unpublished data.

is not complete. Very weakly positive reactions are difficult to evaluate since they may be noted in the presence of complete biliary obstruction, such as that due to cancer. These reactions are probably explained by traces of urobilinogen derived from bile-stained epithelial cells or, in some cases, from bilirubin contained in the serum of blood that has entered the intestines from some source of hemorrhage in a patient with deep jaundice. One such case was seen recently in which it appeared probable that 11 mg. per day of fecal urobilinogen was on this basis. The amount of bilirubin provided by bile-stained mucosa probably never exceeds 5 mg. per day (in terms of urobilinogen), and yet this or smaller amounts may be sufficient to give weak Ehrlich reactions, which are likely to be confusing in diagnosis. If the qualitative test alone is to be used, one should rely only on a series of entirely negative or outspokenly positive reactions in attempting to assay the degree of biliary obstruction. Serial tests are also highly desirable for the urine.

In cases of liver damage, especially cirrhosis, the fluctuation in urobilinogen excretion from day to day, and even at different hours of the day, is often striking. Persistently negative reactions in patients with deep jaundice usually signify complete obstruction, although there are definite exceptions to this. Strongly positive reactions in patients with marked jaundice, but without any suggestion of cholangitis or biliary cirrhosis that might be secondary to a common-duct stone, are nearly always indicative of a parenchymal jaundice, due either to hepatitis or to cirrhosis. In a study of 80 cases of painless jaundice, White⁹⁷ found positive urinary urobilinogen reactions in 38 to 100 per cent, depending on the stage of the disease. This study was carried out with the Wallace and Diamond⁹⁸ method, which is simply a series of dilutions of the qualitative test. In a later paper, White and his associates⁹⁹ compared this method with those of Sparkman¹⁰⁰ and Watson.⁷¹ The former had been proposed as a simpler quantitative method. It employed single samples of urine or feces rather than daily collections. Various disadvantages and errors in this technic were subsequently noted by Watson and Bilde.⁷² In the comparative study of White et al.,⁹⁹ the Sparkman method was found to have no advantage over that of Wallace and Diamond. Neither method was as accurate as the Watson⁷¹ modification of Terwen's¹⁰¹ procedure.

The qualitative test for urobilinogen may be masked by the presence of large amounts of bilirubin, especially when converted to biliverdin, as already mentioned. This is true, however, only

of small amounts of urobilinogen that under ordinary circumstances give but a weak (light-pink) reaction. In cases in which bilirubin or biliverdin might mask a weak reaction, the use of a spectroscope quickly determines the presence or absence of the characteristic urobilinogen-aldehyde band (maximum 565 millimicrons).

A number of substances exhibit yellow, red, or violet reactions with Ehrlich's reagent. These were discussed in detail by Naumann¹⁰² with particular reference to the question of false-positive tests for urobilinogen. In my opinion, these various substances have relatively little practical significance. The color due to indol or skatol disappears when the test is carried out in the proper way with sodium acetate.^{71, 101} I have not encountered false-positive tests due to other compounds with the exception of porphobilinogen,¹⁰³ a substance characteristic of acute porphyria^{103, 104} and readily distinguished from urobilinogen by virtue of chloroform insolubility after forming the Ehrlich compound.¹⁰⁴

Split Products of Hemoglobin or Bile Pigments

Pentdyopent. Prior to Bingold's studies,^{21, 105-108} it was customary to believe that the degradation of hemoglobin in nature went no farther than bilirubin and urobilinogen—in other words, that although the porphyrin ring in the hemoglobin molecule was opened, the four pyrrol nuclei remained intact in a chain. Although this is undoubtedly correct for a major fraction of the destroyed hemoglobin, at least under ordinary circumstances,¹ Bingold's work has clearly revealed that both hemoglobin and the bile pigments may be split *in vitro* to substances with but two, rather than four, pyrrol nuclei. This transition undoubtedly occurs *in vivo* to an extent that is probably variable under different conditions.

Bingold has shown that blood freed of its catalase by heating is readily decolorized by hydrogen peroxide. Subsequent reduction with sodium hydrosulfite ($\text{Na}_2\text{S}_2\text{O}_4$) is then productive of a pink color with an absorption band that, in potassium hydroxide solution, has an absorption maximum at 525 millimicrons. Bingold simply employed this maximum as a descriptive name: "pentdyopent." In ammonia, the maximum absorption is at 540 millimicrons. This reaction has been shown by Fischer and his co-workers^{109, 110} to be due to dipyrromethenes, which are undoubtedly formed during the above procedure by an oxidative splitting in half of the porphyrin ring in the hemoglobin or heme molecule. As excreted in the urine, the dipyrromethene giving the pentdyopent reaction on addition of sodium hydrosulfite is colorless; in other words, it

is excreted as a "propentdyopent." Bingold obtained considerable evidence that the kidney is responsible for the formation of this substance. He noted that in hemoglobinuria the hemoglobin was decolorized by peroxide without preliminary heating, whereas in hematuria heating was necessary, just as it is with human blood. This difference was assumed to be due to removal of catalase by the kidney. Native propentdyopent was observed in urines from many and various pathologic states, but not under normal circumstances. It was found most frequently in urines containing bilirubin, and since the latter has been shown to give the pentdyopent reaction itself, the possibility exists that the main source of the propentdyopent is bile pigment rather than a direct oxidation of the hemoglobin. Bingold states specifically, however, that the reaction has been observed when bilirubin was absent. It should also be noted that urobilin IX α is readily converted to pentdyopent, whereas stercobilin is not.¹⁰⁹ Thus, it is quite conceivable that any urine sample containing mesobilirubinogen may also contain propentdyopent, if one assumes that a part of the former substance has been oxidized in the kidney.

The clinical significance of the pentdyopent group remains to be determined. Preliminary studies intended to provide a quantitative procedure have shown only that this will be attended with numerous and perhaps insurmountable difficulties, owing principally to the instability of the color. There is little doubt that the substance deserves further study, especially regarding its importance to the whole problem of hemoglobin metabolism. The main question to be answered is whether any appreciable fraction of the destroyed hemoglobin is ever excreted as propentdyopent. From time to time, a perplexing situation is encountered in which ordinary studies of blood destruction fail to reveal the fate of considerable amounts of hemoglobin.

In a twenty-eight-year-old patient with Hodgkin's disease, fever and severe anemia, the hemoglobin was 5.65 gm. per 100 cc. During the next nine days, 2400 cc. of blood (equivalent to 260 gm. hemoglobin) was given in nine separate transfusions, at the end of which time, the hemoglobin was 5.75 gm. per 100 cc. The F.U. averaged 515 mg. per day total excretion (equivalent to 167 gm. hemoglobin), and the urine showed small amounts of bilirubin and urobilinogen; in addition, urine pentdyopent tests, performed every other day, were positive. The fecal urobilinogen in the above case clearly indicated a hemolytic process, but failed to account for approximately 100 gm. of transfused hemoglobin. Although the blood volume was not determined, it is unlikely that it could

have increased sufficiently to account for the discrepancy. In any event, the repeatedly positive pentdyopent reactions in such a case indicate the need for further study of this question.

Myobilin and mesobilifuscin. Until very recently, excretory products of muscle hemoglobin were unknown. Siedel and his co-workers^{111, 112} have therefore opened a new field of investigation in their descriptions of a dipyrromethene isolated from the feces in certain conditions. Meldolesi, Siedel and Möller¹¹² first reported the excretion of a substance designated as "myobilin" in the feces of patients with progressive muscular dystrophy. This pigment was characterized by a brown color and a spontaneous green fluorescence (without zinc). The latter disappeared as the pigment was purified, and it was subsequently shown that the fluorescence was related to a combination of the pigment with protein. The substance was not detected in the urine, and it was thought that this was because the chromoprotein molecule was too large. No mention was made of its presence in the bile or of how the molecule was excreted by the liver. Interestingly enough, large amounts of the pigment were found in the feces of women during the first week of the puerperium, in whom it was thought that the pigment was derived from the myohemoglobin of the involuting uterus; in the patients with muscle atrophy or dystrophy, it was ascribed to the loss of hemoglobin from the voluntary muscle. The marked increase of myobilin in the feces was correlated directly with the hemoglobin-poor muscle.

After removal of the protein from the myobilin molecule, the underlying pigment was found to be a dipyrromethene, which was identified with mesobilifuscin, a substance that is dark brown, and does not fluoresce either spontaneously or with zinc; the zinc compound is relatively insoluble. The pigment could not be crystallized. These characteristics are entirely similar to those of the substance described several years ago under the name of "copronigrin," a brownish-black pigment obtained from the feces and characterized by an insoluble zinc compound.⁵⁴ It was recognized later that an entirely similar material could be obtained by oxidation of urobilin or stercobilin.¹ This is also quite in accord with the finding of Siedel et al.¹¹² that mesobilifuscin is present in the oxidized amorphous material (the so-called "Körper II") remaining after the reduction of bilirubin to mesobilirubinogen.

It is obvious that these newer studies raise many questions regarding not only the relatively unexplored field of myohemoglobin metabolism but also the whole problem of the bile pigments.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28451

PRESENTATION OF CASE

A forty-two-year-old housewife was admitted to the hospital because of high blood pressure and a cough productive of small amounts of blood.

Four years prior to admission the patient had a "dizzy spell." Because of an elevation of blood pressure and increased hair about the face her physician sent her to another Boston hospital for adrenal studies. On admission at that hospital her blood pressure was 225 systolic, 150 diastolic. Peri-adrenal air insufflation studies and bilateral adrenal explorations were made. The adrenals were said to have been normal, and no ovarian tumors were felt. Owing to wound sepsis complicating the postoperative course, the patient was hospitalized for more than a month. At the time of discharge her blood pressure was 160 systolic, 110 diastolic. She soon became active again and remained so until one year prior to admission. At this time, after working rather hard in the garden, she began to cough up a "bloody sputum." At this time she noticed some blurring of vision. After approximately two weeks, these symptoms subsided and she seemed well. Two or three months before entry she developed exertional dyspnea and vision was again impaired, and six weeks before she had another episode similar to that noted a year previously; cough productive of bloody sputum continued to the time of admission. During this last attack, dyspnea became progressively worse and at times she noted "attacks of feeling as if there was a weight on the chest." During the week prior to admission there was mild ankle edema. She had been taking 1 tablet of digitalis each day during the six months before entry to this hospital.

The family history was noncontributory. There were two uncomplicated pregnancies eighteen and twelve years before entry.

Physical examination revealed a fairly well-nourished woman sitting up in bed and obviously making no attempt to minimize her discomfort. The skin seemed exceedingly thin and atrophic. The facial hair was noticeable but not heavy. Respirations were rapid but apparently not labored. There was questionable cyanosis of the lips. The neck veins were moderately distended.

Both optic disks were blurred. There was a marked arteriovenous nicking, and there were several small flame-shaped areas of hemorrhage in the right fundus. The anteroposterior diameter of the chest was slightly increased. The left side seemed to lag a bit with inspiration. At the left base posteriorly there were dullness to percussion, absent tactile fremitus, decreased vocal fremitus and diminished breath sounds. These signs disappeared toward the axilla. Over the lower half of the right lung posteriorly there were a few coarse rales. The heart was moderately enlarged to percussion, and the sounds were of fairly good quality. No murmurs were audible. There was marked tenderness in the right upper quadrant. The liver edge could not definitely be felt, but dullness was percussed below the costal margin. There was moderate clubbing of the fingers—the patient indicated that her fingers had always had this shape and that her father's fingers had a similar shape. The examining physician added the note that on observing her raise the bloody material it did not seem to come from the lungs.

The blood pressure was 220 systolic, 140 diastolic. The temperature was 99.6°F., the pulse 90, and the respirations 25.

The examination of the blood revealed a red-cell count of 3,900,000, and white-cell count of 12,900 with 72 per cent polymorphonuclears. The hemoglobin was 60 per cent. The urine was alkaline in reaction, had a specific gravity of 1.010 and gave a +++ test for albumin; the sediment contained a rare red blood cell and a few white cells per high-power field. The blood Hinton test was negative. The blood nonprotein nitrogen was 40 mg. per 100 cc., and the serum protein 7.2 gm., with the albumin 2.2 gm. and the globulin 5.0 gm., making a 2.4 ratio. The van den Bergh test was normal. The prothrombin time was 30 seconds (normal, 25 seconds). The cephalin flocculation test was 0 at 24°C. and \pm at 48°C. The fasting blood sugar was 145 mg. per 100 cc. The 17-ketosteroids excretion in the urine was 2.4 mg. every twenty-four hours. A urine culture revealed nonhemolytic streptococci. An electrocardiogram demonstrated a normal sinus rhythm with a rate of 86. The PR interval was 0.16 second. There were left-axis deviation, depression of the ST segment in Leads 2 and 4, and a diphasic low T wave in Leads 1 and 2. Repeated studies of the basal metabolism revealed rates ranging from +31 to +56 per cent.

An x-ray film of the chest showed spotty hazy areas of increased density throughout the midlung fields, more marked on the right side. There was a small amount of fluid at the right base, and a larger amount at the left costophrenic angle. The

aorta was calcified but not dilated. The heart was enlarged, chiefly in the region of the left ventricle. An intravenous pyelogram showed normal kidney outlines and poor dye excretion.

The patient was treated with digitalis and Mercupurin without much improvement. On the fifth day after admission, in preparation for a phenosulfonephthalein test, 1000 cc. of water was administered by mouth. This resulted in early anuria and later in dysuria. The next day, one hour following the administration of an evening sedative (3 gr. of Amytal), she became irrational and restless. Cheyne-Stokes respirations developed a half hour later. A stomach lavage stopped the irregular respirations, but two hours later these recurred. Ten cc. of aminophyllin was administered intravenously and permanently stopped the Cheyne-Stokes respirations.

Two days later she complained of severe back pain, which radiated to the left. The urine had a specific gravity of 1.020 and gave a +++ test for albumin and a ++++ test for diacetic acid, and the sediment contained 1 red cell and 1 white cell per high-power field. Catheterized specimens of urine examined on the succeeding days contained many red cells and occasional white cells. No casts were found. The blood chloride was 92.5 milliequiv., and the bicarbonate 26.0 milliequiv. per liter. At this time the temperature was slightly elevated, reaching an evening peak of 100°F., and she complained of generalized aches and pains. Another chest roentgenogram still showed the same findings. On the nineteenth day after admission the patient said she felt poorly and complained of some nausea. Three days later she suddenly collapsed and had generalized convulsions. These ceased in a few seconds. When seen by a physician she was cyanotic. The heart sounds were inaudible, but feeble gasping respirations were present. She died within three minutes of the observed onset of the attack.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON: I might interpolate here that one would be anxious to know whether these clubbed fingers showed a softening at the base of the nail, so that when you pressed them the nailbed seemed to be slightly afloat, because I do not believe you ever see that in congenitally clubbed fingers. I am going to disregard this finding.

The blood was slightly hypochromic, which probably is not significant.

I should like to see the chest plates.

DR. GEORGE W. HOLMES: The films cover a period of a little over a month. One film of the chest was taken in June, and the others in July. It

is obvious that there is a lesion in the chest. The process is at the base of the lung, more on the right than on the left. It is accompanied by a moderate enlargement of the heart, chiefly to the left in the region of the ventricle. This second film was taken with a Bucky diaphragm and overexposure to bring out the character of this process in the lower part of the chest. I think the bronchial shadows are enlarged. In other words, this looks like a bronchiectasis so far as the chest films go. I do not see any definite evidence of fluid. My interpretation may be wrong, but that is the first thing I should think of.

DR. RICHARDSON: How about congestion due to cardiac failure?

DR. HOLMES: I should not think so. In the first place, the heart does not have the shape seen in cardiac failure. There is some dilatation, but it does not look like a failing heart. The auricles are not dilated enough to account for the change in the lung fields.

DR. RICHARDSON: It is not the condition of localized edema associated with renal failure that we have been shown by Drs. Szbatzki and Scott?*

DR. HOLMES: It does not look like it to me.

DR. RICHARDSON: I was caught on that before.

DR. HOLMES: There is such a thing; I cannot say that it is not present, but my impression is that it is not. In the films taken of the abdomen, the kidney outlines are quite evident on both sides and the right kidney is distinctly larger than the left but both of them, I think, are within normal limits. Such a slight difference in size would not mean anything definitely abnormal.

DR. RICHARDSON: Supposing you were thinking in terms of myeloma kidney, do you see anything suggestive there?

DR. HOLMES: I should expect them both to be enlarged in that case. The most likely interpretation of the kidneys is that the right was not functioning well and that the left kidney had undergone compensatory hypertrophy. The liver shadow is well seen, and this, I think, is the spleen. If it is spleen, there is no definite enlargement, nor do I think that the liver is enlarged.

DR. RICHARDSON: But you would not say that it was small?

DR. HOLMES: No. Of course, x-ray evidence of change in the size of the spleen is not accurate. But I certainly should not interpret that as being particularly abnormal.

So far as the excretion of the dye is concerned, it is very poor. If the test was carried out properly, I think we can interpret this as evidence of poor function in the kidney.

*Szbatzki, R., and Scott, A. T. Unpublished data.

DR. RICHARDSON: How about the bone structure?

DR. HOLMES: It is well within normal limits; I do not see any decalcification or any other change.

DR. RICHARDSON: They did not do the skull?

DR. HOLMES: No.

DR. RICHARDSON: In the first place I am going to try to lay this endocrine ghost that has been stalking around through this whole story. It is not clear why they operated on the adrenal glands at the other hospital, whether to look for an adrenal medullary tumor, a so-called "pheochromocytoma," or whether to look for an adrenal cortex tumor. If you glance through the record for evidence of endocrine difficulty you find it but it all points in different directions. In the first place, she had two uncomplicated pregnancies. The menstrual history is not mentioned; with the history of normal pregnancy we probably can consider it normal. We are not sure whether she was amenorrheic at the time of entry. I think facial hair that is noticeable but not heavy is not to be overemphasized. It is a common hereditary characteristic. Thin and atrophic skin may suggest an overactive anterior pituitary gland. The laboratory finding of decreased 17-ketosteroid excretion is absolutely opposed to an adrenocortical tumor and in the opposite direction from the increased basal metabolic rate. I cannot see how one can talk about Cushing's syndrome in this case by any stretch of the imagination just because she has a little hair, hypertension and slight anemia. I cannot explain, incidentally, the lowered ketosteroid excretion by any theory. I do not know much about endocrine disease, but I will say that I doubt that Dr. Mallory will find any very striking primary disease involving the endocrine glands.

There are two ways of attacking this problem, one from a purely clinical angle and the other from the laboratory findings. If I take the clinical angle alone, I think this patient had hypertensive heart disease, cardiac failure and renal failure, probably secondary to renal congestion; and the manner of death, although rather sudden with convulsions, is best explained on the basis of cardiac failure or some vascular difficulty. If I look at the laboratory side of it, I am going to get into trouble. She had a mild anemia, possibly accountable on the basis of some renal failure and her general condition. Then there was this serum protein of 7.2 gm. per 100 cc., which is on the high side of normal, particularly since the normal values have recently been running about 6 gm. or a little over. At any rate, the globulin is markedly and definitely increased.

One cannot take too seriously any single laboratory finding, but I think one has to take this seriously. When I try to figure out what diseases produce increased globulin to this extent, there are not many that I have to mention. Certainly not cholera or lymphogranuloma inguinale; and I do not believe that sarcoid would kill the patient. I come down to two causes that seem likely—multiple myeloma and some disease of the liver like cirrhosis.

I get all balled up with electrocardiograms, but I do not see anything specific here. I shall ask Dr. Harwood to give an opinion, but before he says anything, I shall say that the tracing is consistent with hypertensive heart disease and failure.

DR. REED HARWOOD: I agree.

DR. RICHARDSON: Dr. Holmes bothers me by not being willing to say that the x-ray findings might be related to cardiac failure.

DR. HOLMES: I should not say that they could not be. On the other hand, I think they are less likely to be that than something else.

DR. RICHARDSON: Regarding the clubbed fingers, I remember a recent case in which they were very important in connection with bacterial endocarditis, but I cannot see that this case hooks up in any way with bacterial endocarditis. I considered the question of periarteritis nodosa or some similar vascular disease, but I do not see any point in talking about that without more definite evidence. You can have renal and vascular changes in periarteritis nodosa, but not necessarily hypertension and usually more fever. In this case the whole story does not seem to me to fit that sort of disease. So that I have come down rather reluctantly to two diagnoses. One is hypertensive heart disease, with some question in regard to what the kidneys might show,—probably congestion of the kidney with failure and rather fine vascular changes,—with perhaps some vascular changes in the brain, possibly small areas of hemorrhage, and with cirrhosis of the liver on some basis either entirely incidental or possibly the "rare bird" that I almost never see and talk too much about—cardiac cirrhosis. That is one possibility. The only other thing I can do is to say that this patient had a plasma-cell myeloma with myeloma nephrosis, renal failure, hypertension on this basis and the train of symptoms following hypertension with combined renal and cardiac failure. I have not seen many of these cases, but to me they showed renal failure much more clearly than this patient showed. The only things in favor of it are the high globulin, the poor renal excretion of dye and the albuminuria. Bence-Jones protein was not looked for. Since I put myself on the horns

of that dilemma, the obvious thing to do is to take the common disease, and I am going to say that this patient's difficulty was routine hypertension resulting in cardiac failure and mild renal failure, largely on a congestive basis, with vascular changes in the kidneys and cirrhosis of the liver (? "cardiac").

DR. TRACY B. MALLORY: I should like to ask Dr. Holmes if in the last film he can see anything in the superior mediastinum.

DR. HOLMES: I can see something in the last film that is not in the first. It is beneath the clavicle on the right side. It did not impress me.

DR. MALLORY: You do not care to go farther?

DR. HOLMES: Recently we have seen a series of cases with shadows of that kind, which turned out to be due to the innominate artery. Most of them are normal. They are usually caused by tortuosity of the aorta. Aneurysm of the innominate artery, however, can produce such a shadow, as can a large peritracheal lymph node.

CLINICAL DIAGNOSES

Hypertension.

Hypertensive and coronary heart disease.

Coronary occlusion.

DR. RICHARDSON'S DIAGNOSES

Hypertension.

Hypertensive heart disease.

Congestive failure.

Vascular nephritis (slight).

Cirrhosis of the liver (? "cardiac").

ANATOMICAL DIAGNOSES

Dissecting aneurysm of aorta, with rupture into mediastinum and left pleural cavity.

Hematoma, left.

Hypertrophy of heart, hypertensive type.

Arteriosclerosis, marked: aorta.

Pyelonephritis, chronic, inactive.

Cystitis, acute.

PATHOLOGICAL DISCUSSION

DR. MALLORY: When this patient first came in, she obviously impressed everyone who saw her as the complaining sort. Consequently from then on when she had discomfort they discounted it heavily. She did complain bitterly of pain in the back, and the note in the record reads, "Patient complains of pain in the back, probably postural." Nothing was done about it. In another note, it is stated that she complained of aches and pains all over but apparently no specific inquiries were made as to where they might or might not be. That is unfortunate because she unquestionably did have severe pain in the back, owing to a dis-

secting aneurysm. The dissection had evidently occurred some time before death. The day on which she complained of severe back pain was fourteen days before death, and the blood in the outer channel was not merely clotted but partially organized. It was also evident that at the time of or immediately following the initial attack of dissection the outer wall had torn slightly; this resulted in a leakage of blood into the superior mediastinum, where a hematoma of considerable dimensions was present, which likewise showed organization. This must have been present at the time the last chest film was taken.

The terminal episode in this patient was a further rupture of the outer layer into the mediastinum and hence into the left pleural cavity, which contained 2500 cc. of fresh blood.

The kidneys were interesting. They were somewhat small, weighing 250 gm., but markedly scarred, and both showed an extremely severe vascular disease with disproportionate destruction of the tubules as compared with that of the glomeruli. Whether it was entirely a vascular nephritis or whether there was an underlying old pyelonephritis, I am not certain. I am tempted to believe this was hypertension based on a long-standing and inactive pyelonephritis.

The terminal changes in the urine,—the occurrence of numbers of red cells and so forth,—I think was not due to any interference with their blood supply by the dissecting aneurysm but rather to the development of acute hemorrhagic cystitis, which was merely a terminal complication.

The liver showed a very mild chronic type of congestion and by no stretch of the imagination could you call it "cardiac cirrhosis." The bone marrow showed no plasma cells. The lungs showed a little emphysema and fibrosis, so the pulmonary changes were not entirely due to congestive failure. We did not find any clearly defined bronchiectatic cavities, however, so I am left with absolutely no explanation of the elevated globulin and reversed albumin-globulin ratio. We found no evidence of endocrinopathy; the pituitary, thyroid and adrenal glands and the ovaries were all quite normal.

CASE 28452

PRESENTATION OF CASE

First admission. A fifty-eight-year-old physician was admitted because of diarrhea and pain in the right lower quadrant.

For fifteen years prior to admission the patient stated that he tended to have frequent episodes of diarrhea approximately every two or three weeks, each lasting two or three days. These

were usually accompanied by gaseous eructations and sometimes by a spell of vomiting. Occasionally there was a coincident fever. Hypogastric cramps occasionally accompanied the diarrhea, and often these were localized in the right lower quadrant. There was some mucus in the stools, but they were never tarry and did not contain blood.

In addition to the fairly mild episodes in which he had three or four loose movements each day, he had two acute attacks, one six years and another eight weeks before entry, in which he was prostrated by acute abdominal cramps, nausea, vomiting, very frequent watery stools, fever and an initial chill. The most recent episode began about twenty hours before admission when, following a hearty dinner, he began to have watery stools, vomited, retched several times and had generalized abdominal cramps. There was apparently no fever. He had a miserable night but felt better the next morning. During the next day he had two formed stools but later in the afternoon he had a shaking chill. His physician reported that his temperature was 103°F. There was no further diarrhea. The patient believed that oranges or pineapple juice, onions, and fresh fruits in general upset him and initiated the diarrhea. There was no weight loss.

The family history was noncontributory.

The patient had had a severe attack of scarlet fever at the age of fourteen, followed by nephritis, which later went into a nephrotic stage with persistent albuminuria for more than twenty years. He believed that he had had no albuminuria during the subsequent twenty-two years. He had taken several trips to the West Indies within the previous ten years, and on one occasion had had an attack of diarrhea that lasted only one night. Four years before entry, he had an attack of severe substernal pain after walking four blocks. This lasted five minutes and never recurred. Eight weeks previously, during the attack of diarrhea, his heart rate jumped to 180 but returned to a normal rate after pressure was applied to the carotid sinus. He had been taking some alkali in recent months for gaseous eructations and "heart burn."

Physical examination revealed a slightly flushed, obese man in some discomfort. The examination of the heart and lungs was negative except for scattered fine moist rales audible over the posterior bases of both lungs. The abdomen was soft and protuberant. There was no rigidity, and no masses were felt. There was a slight amount of tenderness over most of the right lower quadrant. No costovertebral tenderness could be elicited. The peristaltic sounds were hyperactive.

No tenderness was found on rectal examination, and the prostate was not enlarged.

The blood pressure was 142 systolic, 82 diastolic. The temperature was 98°F., the pulse 110, and the respirations 20.

The examination of the blood revealed a hemoglobin of 14.7 gm. and a white-cell count of 14,100 with 92 per cent polymorphonuclears, 6 per cent lymphocytes and 2 per cent monocytes. Twenty-four hours later the white-cell count had dropped to 11,400 with 71 per cent polymorphonuclears. Further white-cell counts showed figures consistently less than this. A blood Hinton test was negative, as was the urine examination. The blood nonprotein nitrogen was 22 mg. per 100 cc. The stool was greenish brown and guaiac negative; no amebas or amebic cysts were seen. An electrocardiogram demonstrated a normal sinus rhythm of 100 and slightly lowered T waves.

A flat plate of the abdomen showed what was interpreted as tuberculous lymph nodes in the right lower quadrant. There were no abnormal gas or soft-tissue shadows. The kidney outlines were normal. There were no shadows present that could be interpreted as stones. A barium enema showed that the colon filled readily; there were no constant irregularities or filling defects. About 15 cm. of the terminal ileum filled, and there was a constriction in its terminal portion opposite the tip of the cecum. The appendix was not visible. Practically all the barium was evacuated. Later a barium meal revealed a small hiatus hernia and fairly persistent spasm of the antrum of the stomach and the pyloric valve. The stomach and duodenum were otherwise normal. Serial examinations of the small bowel revealed no evidence of obstruction, but the constriction in the terminal ileum was again demonstrated. The mucosa at the site of the constriction was distorted and appeared to have been destroyed over an area less than 1.0 cm. in length. The cecum did not remain filled completely, there being a gap between the terminal ileum and transverse colon producing the so-called "Stierlin sign." The mucosa of the cecum and ileum appeared normal. The appendix did not fill. There was no dilatation of the small bowel.

The stools were repeatedly examined for the presence of amebas and amebic cysts, employing the zinc sulfate flotation method, but without success.

After nine days of hospitalization the patient was discharged without an established diagnosis. He was told to return after a month of rest for an exploratory abdominal operation.

Second admission (one month later). Following discharge the patient had felt well. During

the interval he had not suffered with tenesmus, cramps or diarrhea.

There was no definite change in the physical examination, and on the second day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CLIFFORD FRANSEEN: This case, in summary, resolves itself into the differential diagnosis of lesions of the terminal ileum that are chronic and produce partial intestinal obstruction or perhaps chronic or recurring intussusception in a man of fifty-eight. Except for the findings in the right lower quadrant, the data do not seem to be relevant. The history, of course, is important, especially the fifteen-year duration, if one is going to try to make a single diagnosis that will explain the symptoms over all these years. Throughout this period he had recurrent inflammatory episodes and obstruction, cramps, nausea, vomiting, watery stools and so forth. One must depend on the x-ray findings in the right lower quadrant because he had no palpable mass.

The diagnoses to be considered are several. The first thing that suggests itself from the x-ray findings is tuberculous nodes in the right lower quadrant. Presumably the record means that calcified nodes were found. These can occur coincidentally in a large number of people of this age in x-ray examinations for other conditions, and alone they do not establish the diagnosis. Similarly, the appendix did not fill. In a large percentage of patients of this age who have routine examinations, I am quite sure the appendix does not fill, and it may not be important in this case.

I wonder if we may see the x-rays before we go any farther.

DR. RICHARD SCHATZKI: This is the barium enema, and this represents the small area of narrowing that is described in the record. It is about 1.5 to 2.0 cm. in length and is constant because the film taken after evacuation also shows it. I should agree with the record that the mucosal pattern is markedly distorted and that the mucosa seems to be destroyed. This is another set of films taken after the oral administration of barium, and you can see this same area again. It is certainly a well-localized destruction of the ileum.

DR. FRANSEEN: Would you care to say a word about Stierlin's sign?

DR. SCHATZKI: I think what the examiner meant is what a Swiss roentgenologist described thirty years ago—namely, a constant failure of the cecum and of the adjacent part of the ascending colon to fill during barium examination by mouth, in association with tuberculosis of the ileocecal re-

gion. I should say this was suspicious of it but by no means definite.

DR. FRANSEEN: This could be present in any condition that gives spasm of the cecum?

DR. SCHATZKI: Very definitely so. The record does not say anything about the cecum, but it appears normal so far as I can see.

DR. FRANSEEN: Is that area at the lower end of the cecum significant? It does not show the same smooth outline as the rest.

DR. SCHATZKI: It looks quite normal on the postevacuation film, however.

DR. FRANSEEN: To go back to the things we have to consider. First, we have tuberculosis. Are these the calcified areas here?

DR. SCHATZKI: Yes.

DR. FRANSEEN: They are calcified retroperitoneal nodes. If one considers a tuberculous process that has gone on over a period of fifteen years, it seems to me that one would expect to find more than is seen here. This lesion appears primarily to involve the ileum, over a relatively short segment, and not the cecum. After fifteen years one would have expected an inactive process, probably a cicatrizing lesion, which might simulate this condition.

I am trying to recall an interesting case in a man somewhere around fifty years of age that we had three or four years ago. The only lesion he had was a minute constricting area some distance from the ileocecal valve. If I had not known of that case I should not be suspicious of this area as being due to tuberculosis. It is my impression that tuberculosis is primarily an ulcerating process and would occur most likely in a younger man.

The next thing to consider, of course, is regional enteritis. It, too, is a disease of youth. I personally do not remember any case in a patient as old as this man, nor do several of my colleagues whom I questioned. Regional enteritis usually occurs in patients under forty. It is primarily a disease of youth, and probably of not so long duration as this condition, which has gone on for fifteen years. It also seems likely that if it had gone on to this stage of intestinal obstruction a mass would have been found, which is not true. Furthermore, the typical x-ray appearance of the bowel with the usual string sign is not present. The last patient I saw who had the string sign was a man of forty who proved to have an adenocarcinoma, so that sign may also be misleading. I should not consider regional enteritis seriously for these reasons.

Other inflammatory processes must be discussed because there were recurrent episodes. An appendix abscess sometimes produces bizarre findings, but under this diagnosis one would have to

make some other explanation for the episodes preceding the present one unless the patient had an obscure chronic appendicitis associated with obstruction. Also, no mass was palpable, so that there is not much reason to consider appendix abscess in this case.

One must, of course, consider a tumor. The malignant tumors that perhaps most frequently involve this segment of the bowel are sarcomas of the small intestine, carcinomas and lymphosarcomas. Lymphosarcoma would probably involve a larger area. The long duration is against malignancy unless it had been superimposed on a benign condition over these years. One might consider that the repeated episodes of obstruction were caused by intermittent intussusception or partial intestinal obstruction by some benign tumor in this region, but the usual benign tumors, such as lipomas, xanthomas and fibromas, are ordinarily somewhat pedunculated and are not circular and constricting as this lesion appears to be. The only other condition that I can consider in which one could have a benign tumor which would gradually advance and produce this picture is a carcinoid. The small intestine is the commonest site of carcinoid, except the appendix. In this case, one might suppose that the appendix was the primary site of the carcinoid and that the area in the ileum was involved secondarily, but I think that a primary carcinoid of the ileum is more probable. That would fit in best with the history of fifteen years' duration, because these tumors grow very slowly; however, I do not know of any case of carcinoid with such a long duration. It is conceivable that it might occur because other similar benign conditions can go on and produce symptoms like these until the final episode of more complete obstruction. The patient was in the age group in which carcinoid commonly occurs—another point in its favor. Likewise, the mass was small. Carcinoids can, of course, grow to considerable size and metastasize.

I should have to use carcinoid of the ileum as the diagnosis best fitted to this case. Tuberculosis cannot be entirely excluded, but I think it is unlikely.

DR. SCHATZKI: If our impression is correct that the mucosa was destroyed, does that not argue against the diagnosis of carcinoid?

DR. FRANSEEN: Yes; but that is at variance with the opinion given in the abstract. It says that the area was possibly destroyed over an area 1 cm. in length, which would be consistent with carcinoid. Of course, if the carcinoid had become malignant, the destruction of the mucosa would be consistent.

DR. SCHATZKI: I do not know the answer, but I should say from looking at the films that the mucosa was destroyed.

DR. FRANSEEN: That would be very much more in favor of a malignant process, possibly carcinoma.

DR. MALLORY: Even in cases in which carcinoids have become invasive and have metastasized to the regional lymph nodes we have not seen even one case with ulceration in the mucosa. It grows in a disk-like form in the submucosa and never spreads through to the surface.

DR. FRANSEEN: But when carcinoma intervenes, what occurs?

DR. MALLORY: That does not happen. A carcinoid is not an epithelial tumor and never turns into carcinoma. It is potentially a malignant tumor in its own right but does not become a carcinoma: it remains an argentaffine tumor.

DR. FRANSEEN: I understand that is a disputed point among pathologists. You believe that it does not become carcinomatous?

DR. MALLORY: Yes; Masson showed very definitely that it is a tumor of some peculiar nerve end organ rather than a tumor of the epithelium.

CLINICAL DIAGNOSIS

Regional enteritis?

Tuberculosis?

Appendix abscess?

DR. FRANSEEN'S DIAGNOSIS

Carcinoid of ileum, probably malignant.

ANATOMICAL DIAGNOSES

Appendicitis, healing.

Inflammation of Meckel's diverticulum, acute.

PATHOLOGICAL DISCUSSION

DR. MALLORY: I am sorry Dr. Arthur W. Allen, who operated on this patient, is not here to discuss the case. On the first entry, the patient was studied by Dr. Allen and Dr. Chester M. Jones and was discharged with three questionable diagnoses: regional enteritis, tuberculosis and appendix abscess. It was eventually decided that the possibility of appendix abscess was great enough so that he should return for operation as soon as he could adjust his affairs, and that was done.

On the second entry he was promptly operated on, and the first thing that popped into sight when the abdomen was opened was a Meckel's diverticulum. A little further exploration showed an appendix buried in adhesions along the brim of the pelvis, with no pus about it and no evidence of abscess. Both the appendix and the Meckel's diverticulum were removed. The surgeon's impression was that the appendix had been recently inflamed and was in a subsiding stage. In the laboratory, we formed another impression.

The appendix did not impress us greatly, and the Meckel's diverticulum contained purulent exudate in the lumen. So we believed there was an acute or still active diverticulitis and that the appendix, which was about two thirds obliterated, had undoubtedly, at various times in the past, been the seat of an inflammatory process but probably not in an extremely recent period. The anatomic findings are difficult to correlate with the x-ray findings, and yet I think we must assume that Dr. Allen was able to rule out such possibilities as tuberculosis, regional ileitis and carcinoid since he had a good exposure of the entire terminal ileum and nothing was found except the Meckel's diverticulum.

DR. SCHATZKI: How far away from the ileocecal valve was the Meckel's diverticulum?

DR. MALLORY: I judge very close, but it was not measured.

DR. SCHATZKI: This lesion is only 5 cm. proximal to the ileocecal valve. That would be very low for a Meckel's diverticulum. Furthermore, I still cannot see a diverticulum.

DR. GLENDY: How often can you demonstrate it?

DR. SCHATZKI: We hardly ever see the diverticulum itself, probably because it looks so much like the intestine. This is particularly true in the usual position of a diverticulum, higher up where it is difficult to distinguish the intestinal loops. But in this case the questionable loop is clearly separated. The diverticulum should have shown up, unless its entrance was closed and therefore did not fill with barium.

DR. MALLORY: The operative note said that the walls about the mouth were very thick.

DR. SCHATZKI: Then that is a possibility; however, the position is unusually low for a Meckel's diverticulum.

DR. GLENDY: Do you think that the diverticulum was close enough to the area of narrowing to produce spasm?

DR. MALLORY: That is my hypothesis. I think anyone has a right to disagree with it. I do not believe we have proved it at all.

DR. FRANSEEN: Spasm could not produce destruction of the mucosa.

DR. SCHATZKI: Obviously, the mucosa was not destroyed, just swollen.

* * *

The following post-conference statement was obtained from Dr. Arthur W. Allen:

I regret having been absent from the clinicopathological conference on Case 28452, because I could have cleared up many of the points that seemed to worry the discussers.

In the first place the patient gave a very atypical story for appendicitis, since in addition to nausea, vomiting and abdominal pain he had profuse diarrhea. This is very unusual in appendicitis because the inflamed appendix usually does not rest near enough to the rectum to produce peristalsis by irritation.

The patient entered the hospital twenty hours after the onset of his episode, and although he had a leukocytosis consistent with an inflammatory process, the abdomen was generally tender and there was no evidence of localization, either abdominally or by rectal examination. Finally, however, he did develop tenderness in the right lower quadrant.

The probability that the condition was due to appendicitis was so strongly considered that the patient was strictly Ochsenized, and he made a fairly prompt response to this treatment. His temperature, having reached 103°F as a peak, came down to normal on the fourth day. Peristalsis, which had ceased after he entered the hospital, again became normal, and food and fluids were resumed by mouth.

The repeated minor episodes, with two previous severe attacks, always associated with a very sensitive colon, made us wonder whether the whole process might be accounted for on some basis other than simple, acute appendicitis. Very careful studies were made, including many stool examinations for amebae, since his first severe episode had taken place while on a Caribbean cruise.

The x-ray examinations were not quite so puzzling to Dr. Hampton and to me as they appeared to be at the time of the conference. In fact, Dr. Hampton thought that appendix abscess explained the situation better than any other diagnosis. After the febrile reaction had quieted down, there was a very definite, although ill defined, mass which could be felt bimanually in the right side of the abdomen, and the patient was discharged with a diagnosis of appendicitis with peritonitis, to return for deliberate appendectomy after four weeks.

The findings at operation are not described well in the abstract, owing, I am sure, to our own carelessness in dictating the operative note. The Meckel's diverticulum was not adherent to any structure, it had no appearance whatever of acute inflammation, and the fact that it was found acutely inflamed by pathological examination does not indicate that this had anything to do with the acute episode six weeks previously. The appendix, however, was lying in the pelvis next to the rectum and was adherent to it, and when it was elevated out of the pelvis, it was obvious that we were freeing fresh, more recent adhesions. The distal half of the appendix was thickened and reddened, and appeared exactly like many I have removed several weeks after a known acute inflammatory attack.

There was no doubt whatever in my mind or in my assistant's mind that the appendix had accounted for the patient's acute attack and that the Meckel's diverticulum was, in fact, an incidental finding.

The patient's convalescence after operation was identical with the type that goes with an appendix removed under these circumstances; in other words, there was more febrile reaction than in the removal of an interval or normal appendix, and considerably more ileus than is usually seen. This might have been due to the added removal of the Meckel's diverticulum, but I believe is more likely to have been due to the stirring up of the quiescent infection in the pelvis.

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THE ONE-DAY CURE FOR SYPHILIS

It is surprising that the *Reader's Digest*, which renders a notable service with its excellent summaries of current magazine articles and new books, should publish for lay consumption an article* on a new one-day cure for syphilis as if the procedure were already available for every physician to use as safe and scientific on any and all patients with syphilis.

Such an ill-advised statement has raised many false hopes and disturbed many patients who are progressing satisfactorily under treatment. It has instigated many queries to physicians and medical journals about a method that is still in the experimental stages. The method has very definite

hazards. Not everyone can tolerate a fever of 106°F., and patients with certain defects should never be exposed to such a temperature. The apparatus and controls are not at hand. Neither physicians nor nurses have had sufficient training in the method. Too few cases have been treated and too short a time has elapsed to know if there are any late serious effects of the treatment and if the results on the disease are permanent. It may be a step forward in the treatment of syphilis, but much experimental work must be done to be sure that this particular technic is the proper procedure for every case of syphilis. There are many pitfalls in this complicated program, and it is cruel for a scientifically trained writer to propose such a method to the public as accepted and readily available in every city and town. Furthermore, why did this writer pick out an eleven-year-old article to stress the bad effects of routine anti-syphilitic treatment? In a letter published in the September 19 issue of the *Journal of the American Medical Association*, Dr. Harold N. Cole, a distinguished syphilographer and the author of the former article, emphasizes the bad effects of publicizing prematurely an experimental procedure that needs confirmation before it is widely available for syphilis in general.

Physicians can assure their questioning patients that the one-day treatment is in the experimental stage and is not a safe and sure procedure and that it will eventually be made readily available if scientific evidence warrants its acceptance. Incidentally, one cannot refrain from suggesting that the publication of medical articles in a periodical for lay consumption is a great responsibility and one that cannot be discharged properly without the aid of competent medical opinion.

GUIDES TO THERAPY FOR MEDICAL OFFICERS

AN excellent pocket-sized technical manual, entitled *Guides to Therapy for Medical Officers*,† has recently been issued by the War Department. As

*de Kruif, P. Fouod: a one-day cure for syphilis. *Reader's Digest*, September, 1942.

†War Department. Technical Manual 8-210. *Guides to Therapy for Medical Officers*. 185 pp. Washington: Government Printing Office, 1942.

stated in the opening paragraph, the purpose of this manual is to provide the medical officer with a handy text containing guides to therapy under emergency conditions or in diseases with which he is relatively unfamiliar. The accepted treatment of the diseases commonly encountered in civilian life is not discussed, nor are such topics as the control of communicable diseases and sanitation. In other words, it is intended to serve as a guide to the "general practitioners" of the Army and not as a text for specialists, who are likely to be stationed with evacuation units or in general hospitals. It is also emphasized that the text does not comprise rules and regulations that must be followed, but merely suggestions to be used at the discretion of the medical officer.

The manual is well conceived and carefully executed. The Surgeons General of the Army and Navy, early in 1940, requested the Division of Medical Sciences of the National Research Council to establish committees that should act in an advisory capacity to the two medical corps. Much of the text of this manual is based on material compiled by these committees. Final revision was conducted by pertinent divisions of the Office of the Surgeon General, United States Army. The manual was edited by a member of the Committee on Information of the National Research Council.

The reports of the many experts are presented in an easily readable, compact and orderly fashion. The major subjects covered are as follows: surgical emergencies; medical emergencies; diagnosis and treatment of venereal diseases; chemotherapy and serotherapy in certain infectious diseases; treatment and control of certain tropical diseases; and rickettsial diseases. The contributors to each of these sections include many of the leading names in American medicine and surgery.

Under surgical emergencies are included the commonest types of wounds in various parts of the body, the management of shock and the early treatment of burns. Most of the essential details are given, but the specialized forms of treatment that can be undertaken only by experts are almost entirely omitted. The section on medical emer-

gencies covers the majority of situations that might arise under the great variety of conditions to which troops are likely to be subjected, including such diverse items as acute poisoning from various foods, chemicals, plants and animal sources, sea-sickness, altitude sickness, the effects of exposure to heat and cold, starvation and the acute psychoses. The sections on tropical and rickettsial disease are meant to acquaint medical officers with conditions that are rarely encountered in civilian practice but that are very likely to be met with in the far-flung regions where troops may be operating. Each section is preceded by a table of contents, and there is a well-arranged and easily usable index at the end of the volume.

The manual seems well suited for the purposes for which it is intended. In fact, it could advantageously serve as an abbreviated and handy text for general practitioners and for medical students and hospital interns who are likely to see active military service in the near future. It is likewise suitable as a "procedure book" for use in the emergency rooms of general hospitals. No doubt, the manual will be kept up to date when reprinting becomes necessary. It can be obtained for twenty-five cents from the Superintendent of Documents, Washington, D. C.

MEDICAL EPONYM

SCHICK TEST

This was first described by Dr. Béla Schick (1877), then private docent in the clinic of Professor von Pirquet in Vienna, in an article "Die Diphtherietoxin-Hautreaktion des Menschen als Vorprobe der prophylaktischen Diphtherieheilseruminjektion [The Diphtheria-Toxin Skin Reaction in Man as a Preliminary Test in the Prophylactic Injection of Diphtheria Antitoxin]" in the *Munchener medizinische Wochenschrift* (60²:2603-2610, 1913). A portion of the translation follows:

For intracutaneous injection, the ordinary 1-cc. Reckord syringe marked in tenths is needed. The most important part is the needle, which . . . should be as fine as possible, with a short bevel, in order that the opening of the needle may be covered as quickly as possible when it is introduced into the most superficial layers of the skin. A dose of 0.1 cc. of a dilution of the toxin, which must be calculated in each case is

given. As a rule, one fiftieth of the minimal lethal dose for a 250-gram guinea pig suffices—for example, with a lethal dose of 0.005 cc. for a 250-gram guinea pig, an injection of 0.1 cc. of a 1:1000 dilution. If the injection is successful, there is at once apparent a white wheal-like elevation with dots corresponding to the orifices of the hair follicles.

The changes that occur at the site of injection of the diphtheria toxin resemble in appearance those occurring during the first twenty-four to forty-eight hours of a positive tuberculin reaction. . . .

A negative response to the intracutaneous test always indicates the presence of diphtheria-toxin antibodies in sufficient amounts for prophylaxis. . . . A positive test does not indicate their absence with the same certainty, since many individuals, children as well as adults, may show an inflammatory reaction at the site of injection of diphtheria toxin in spite of the presence of protective substances in their serums.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

PNEUMONIA

As the tabulation of medical causes of maternal death printed in last week's issue of the *Journal* shows, pneumonia ranked second to heart disease as a fatal complication of pregnancy. There were 12 cases in which this disease was the primary cause of death during 1941: in 7, the infection followed normal delivery; in 3, the patients died undelivered; and in 2, there had been an operative delivery. Autopsies were performed in 5 cases.

Of the 7 associated with normal delivery, the first case was that of a patient who developed pneumonia on the third post-partum day and died three days later. Autopsy revealed a normal pelvis and bronchopneumonia of the influenza type.

The second patient, when five and a half months along in her second pregnancy, developed pneumonia; a spontaneous abortion occurred the day after hospital entry. The infection was due to a Type 22 pneumococcus, and in spite of sulfonamide and serum therapy, death occurred the following day.

The third patient developed a fever thirty-six hours post partum. Blood cultures were negative; the patient was given sulfathiazole and transfused; a clinical diagnosis of pneumonia was made and confirmed at autopsy.

The fourth patient entered the hospital at term with an acute upper respiratory infection. She had a normal, rapid delivery but died on the tenth post-partum day, autopsy proving the cause of

death to be bronchopneumonia and pneumococcal septicemia.

The fifth patient, who had had thirteen previous pregnancies, entered the hospital cyanotic and with a pulse rate of 140. Ten hours after entry, she delivered herself of a 2-pound infant, and lived but thirty-four hours post partum. A diagnosis of pneumonia was confirmed at autopsy.

The histories of the last two cases in this group are incomplete. One of them entered the hospital with influenza and died during delivery. The other case was that of a patient delivered at full term of a living child who died a few days after delivery.

Of the 3 cases allocated to pneumonia who died undelivered, the first was that of a patient, five months along in her third pregnancy, who died four hours after admission to the hospital.

The second patient entered the hospital at term with acute bronchopneumonia. She had had a cold for three weeks and died undelivered three days after entry. An autopsy was performed, and death was found to be due to bronchopneumonia.

The third patient was a woman who, in the seventh month of her third pregnancy, had called her physician because of a severe cold of three days' duration. She was sent to the hospital, and a diagnosis of bronchopneumonia made by x-ray study. Death occurred four days after entry, and a living child, weighing 6 pounds, 3 ounces, was delivered by post-mortem cesarean section. The causative organism was a Type 3 pneumococcus.

The remaining 2 cases were patients who were delivered by operative intervention. The first case was handled unintelligently: after a sixty-hour labor and an unsuccessful attempt at high-forceps delivery, a cesarean section was done. Pneumonia developed postoperatively. This, of course, was an unjustifiable death.

The second patient was delivered by low forceps. There is no evidence in the record that pneumonia was present at the time of delivery, but two weeks afterward x-ray films showed a bilateral lobar pneumonia, from which she did not recover.

It is very gratifying that only one of these cases was a postoperative pneumonia and that this was the only case associated with unintelligent obstetrics. Those patients who died undelivered emphasize particularly the seriousness of pneumonia as a complication of pregnancy. It must be borne in mind that a cold may develop into bronchitis and bronchitis into pneumonia, and that during pregnancy the patient with a common cold must be treated more conservatively than she would be if she were not pregnant. The attending physician should be notified immediately, and rest in bed should be ordered. A cold accompanied by a fever

requires medical examination. Although chemotherapy and serum treatment have undoubtedly reduced the mortality from pneumonia, both methods to be successful require early diagnosis. Only closest possible co-operation between the physician and the patient will make the treatment of pneumonia as successful as it should be.

DEATHS

ADAMS—**CHARLES W ADAMS, M.D.**, of Cambridge, died October 20. He was in his sixty-fourth year.

Dr Adams received his degree from Harvard Medical School in 1905 and was a member of the Massachusetts Medical Society and the American Medical Association. His widow survives him.

COON—**WILLIAM H COON, M.D.** of Easton, Connecticut, died October 6. He was in his sixty-eighth year.

Dr Coon received his degree from Bellevue Hospital Medical College, New York, in 1897. He had served as assistant physician at the Northampton Insane Hospital, as house officer at the Boston City Hospital as executive officer of the Harvard Infantile Paralysis Commission, and as health commissioner of Bridgeport, Connecticut.

He was a former member of the Massachusetts Medical Society.

His widow, a son and a daughter survive him.

GREENWOOD—**ALLEN GREENWOOD, M.D.** of Boston, died October 23. He was in his seventy-seventh year.

Born in Chelsea, he received his degree from Harvard Medical School in 1889 and served his internship at the Boston City Hospital. Dr Greenwood was professor of ophthalmology, emeritus, at Tufts College Medical School and lecturer on ophthalmology in the Courses for Graduates, Harvard Medical School. He was affiliated with the Boston City Hospital, the Massachusetts Eye and Ear Infirmary, the Beth Israel Hospital, the New England Hospital for Women and Children, Adams House, the Waltham Hospital, the Milford Hospital and the Framingham Union Hospital.

Dr Greenwood was a fellow of the Massachusetts Medical Society and the American Medical Association. He held memberships in the American Academy of Ophthalmology and Oto-Laryngology, the American Ophthalmological Society, of which he was a former vice president, the Association for Research in Ophthalmology, the New England Ophthalmological Society and the American College of Surgeons.

His widow, two daughters and a son survive him.

WALKER—**HARRY A WALKER, M.D.**, of Somerville, died October 30. He was in his sixty-second year.

Born in Binghamton, New York, he received his degree from Cornell University Medical College in 1905. He served for four years in New York hospitals before moving to Somerville, where he was a member of the staff of the Somerville Hospital.

Dr Walker was a fellow of the Massachusetts Medical Society and the American Medical Association. He was a member of the Somerville Medical Society, the Cornell Medical Alumni, and the Cornell Club of New England.

His widow, a son, and two daughters survive him.

WAR ACTIVITIES

SELECTIVE SERVICE

The following announcement by the Massachusetts state director of selective service is of general interest.

It has been decided by National Headquarters, Selective Service, not to extend the program of physical rehabilitation. Further activity relative to this program has been discontinued so far as the Selective Service System in Massachusetts is concerned. The names of those physicians, dentists and institutions who have signified their willingness to participate in a program of rehabilitation will be kept on file at State Headquarters.

This is not intended to affect or interfere with projects or programs for rehabilitation of Selective Service registrants on the part of groups or organizations not directly connected with Selective Service.

Local board examining physicians have been asked to exercise discretion in utilizing the services of examining dentists in the physical examination of selectees. Dental diseases or defects are no longer shown as a cause for rejection by local board examining physicians. Hence the desire to conserve the time and energy of examining dentists who have been so faithful and loyal in their efforts to make a contribution to Selective Service in the field of dentistry. Some local boards have utilized the services of examining dentists in some capacity outside dentistry. This of course permissible and it is not meant that such activities or help is to be dispensed with.

Examining physicians in full co-operation with their local boards are now engaged in reviewing the cover files of all registrants who have been placed in Class IVF because of some physical disqualification. They have been called on to exercise sound medical judgment in studying these records so that those registrants who are hopelessly disqualified for all military duty will be kept at home and all others who are qualified for full or limited military duty will be sent to the induction station.

A study of registrants in Class IVF because of a mental or nervous disorder is about to be undertaken. It will be confined to groups of ten or fifteen registrants from each of fifteen local boards scattered throughout the State in urban and rural areas included. The purpose of this study is to determine what proportion of the registrants in this group are qualified under present standards, for full military duty as well as to discover what number if any now disqualified for military duty are fit subjects for psychiatric or other methods of rehabilitation.

Recently local boards were directed to begin immediate preliminary reclassification of all married men with wives only. This is of immediate and pressing interest to those members of the medical profession who are now in Class IIIA either because of collateral dependents or because they are married and have no children. The demand for medical officers in the armed forces is insistent; it is pressing; it is imperative. Medical men in the two categories named above who have been declared by the Procurement and Assignment Service to be available for military duty should apply at once for a commission through the Medical Officers Recruiting Board, 319 Longwood Avenue, Boston. There is always a chance of delay in processing the papers. Occasionally x-ray and other studies are necessary. Local boards are no longer permitted to defer the induction of a registrant so that he may apply for or await the processing of an application for a commission. If a medical man has delayed in ap-

plying for a commission and his order of induction has been issued, he may be inducted and have to serve as an enlisted man before the commission catches up with him.

As the need for medical men in the armed services is becoming more generally recognized, there has been a noticeable stiffening in the attitude of Selective Service officials toward members of the medical profession who have been declared available for military duty yet who refrain from taking the necessary steps until it is almost too late. National Headquarters, Selective Service System, in Local Board Release, No. 89, has said, in part:

In considering the classification of a registrant who is a qualified medical doctor, dentist or doctor of veterinary medicine, the local board may, if it finds such registrant should not be deferred for reasons other than dependency, take into consideration the pay and allowances which such registrant would receive in the event he is commissioned in the armed forces. In practically all instances the pay and allowances of such registrant, if he were commissioned as an officer, would be sufficient to eliminate the question of dependency.

In this connection, it may be said that it is probable that Selective Service will begin inducting men with dependent wives in the very near future, possibly in November or December, 1942.

If a registrant applies for a commission and he is refused, either because he is found physically disqualified or for any other reason, local boards have been asked to consider classifying him in either IVF or IIA. Class IVF will be restricted to those registrants whose physical examinations by the Medical Officers' Recruiting Board reveal the presence of a physical defect which would normally cause rejection at the induction station.

Students in accredited medical, dental or veterinary schools may apply for a commission in the Medical Administrative Corps as soon as they have been admitted to the freshman class. Local boards have been asked to consider for occupational classification (Class IIA) students who are in good standing in a medical, dental or a veterinary school, as well as those who are in an osteopathic school. This is on the theory that such students are in training for an occupation necessary in the national health, safety or interest.

LIEUTENANT COLONEL VICTOR D. WASHBURN, M.C., A.U.S.
State Medical Officer

38 Chauncy Street
Boston

MISCELLANY

PULMONARY TUBERCULOSIS AMONG SPANISH-SPEAKING PEOPLE

To meet the menace of a rise in the tuberculosis death rate due to war conditions, a renewed emphasis must be laid on special problems in the fight to control and ultimately to eradicate the disease. It is timely and pertinent to call attention to certain of these problems in which assistance of the general medical profession is indispensable.

Industrial problems and racial problems stand out clearly against the background of national health, which is threatened by the exigencies of war. A cogent article (Wilson, W. J. *Pulmonary tuberculosis among the Mexican population of Weld County, Colorado*. *Rocky Mountain M. J.* 39:432, 1942) is illustrative of the situation existing in various parts of this country, one which can only be met by concerted action on the part of the medical profession.

The problem in Weld County, Colorado, differs in extent but not in kind from countless similar ones that confront physicians throughout the country.

* * *

It is a well-established fact that the incidence of pulmonary tuberculosis varies markedly in different races. Roughly, there appears to be an increase in incidence as the pigmentation of the skin characteristics of the race increases, and also an increase with the magnitude of climate change occurring when the darker-skinned races migrate to colder regions. Thus, a native of the tropics coming to Colorado to live is more liable to contract tuberculosis than a native Coloradoan. Whereas the present death rate for tuberculosis in the United States Registration area is approximately 36 (in 1940) per 100,000 population in Whites, the rate for Negroes is almost three and a half times that number.

The incidence of tuberculosis in the Mexican falls between the rates for Negroes and Whites. However, reported figures have shown fairly wide variations. These variations are to be expected, since the Mexican who was born and raised in the Rio Grande valley and who later moves across the river into the Texas side of the valley has made no change in climate at all, but the Mexican who migrates from Monterey to Colorado has made a very decided change. It is therefore expected that the incidence of tuberculosis among Mexicans coming to Colorado will be greater than that among those stopping in southern Texas, New Mexico and Arizona.

The Weld County study, under the joint sponsorship of the Weld County Tuberculosis and Health Association and the Weld County Health Department and Public Health Laboratories, shows the tuberculosis problem that exists among the several thousand Mexicans residing in this Colorado county. Nearly all of them are occupied in farm work, mainly the planting and harvesting of sugar beets. Over half of them live in "Spanish colonies." Living conditions are quite uniformly substandard and crowded. This undoubtedly contributes in no small measure to the picture presented by this study.

During the thirty-month period from September 1, 1939, to March 1, 1942, a case-finding program was carefully conducted among the Mexican population of Weld County. A total of 1745 persons were tuberculin tested, and all positive reactions followed up with an x-ray examination. Of the reported studies, very few have contained complete follow-ups of all positive reactors. The Weld County study is now complete except for the progress following diagnosis and treatment of all active cases found.

The tests were made, for the most part, in "Spanish colonies" after showing a series of educational films produced by the National Tuberculosis Association. The interest response was very gratifying, and all age groups attended, as is shown in the figures of Table 1. The ages ranged from less than two years to over seventy.

The remainder of the persons included in the study were segregated from the testing programs carried on in the schools of the county, and a few persons who were tested for various reasons. On the whole, the group studied should represent a very nearly accurate cross section of the Mexican population of the county.

Of the 1745 persons tuberculin tested, 745, or 42.7 per cent, had positive reactions. These 745, along with forty other persons from families in which active tuberculosis was found, were given chest x-ray examinations. These forty people had not had previous tests.

In 481 of the chest x ray films, there was no evidence of tuberculous activity and they were dismissed from further study.

In 304 cases, radiographic evidence ranged from merely suggestive to definite evidence of disease. These were referred to the Chest Clinic of the County Health Department for further study, including physical examination, sputum examinations and cultures. Sixty-one persons were found to have active pulmonary tuberculosis. Of these, 51 had far advanced disease, 4 had moderately advanced disease, 4 had unusual lesions and 2 refused to co-operate.

Based on this study, the incidence of tuberculosis among the Mexican population of Weld County is found to be the staggering figure of 34.17 per 1000 population — Reprinted, in part, from *Tuberculosis Abstracts*, October, 1942

NOTE

The Salem Tumor Clinic held a teaching clinic at the Salem Hospital, on Friday, October 30, with Dr George W. Holmes, professor of radiology at Harvard Medical School, as the speaker. Dr Holmes spoke on General Aspects of Irradiation in Carcinomas.

CORRESPONDENCE

CAROTID-SINUS REFLEX

To the Editor In an article published in the September 24 issue of the *Journal*, entitled "The Significance of the Carotid Sinus Reflex in Biliary Tract Disease," by Engel and Engel, the authors offer some interesting observations. However, their conclusion that a hyperactive cardioinhibitory carotid sinus reflex in cases of biliary tract disease is due to sensitized nervous pathways is not warranted from their limited observations. Do they imply by sensitized nervous pathways a lowering of the synaptic resistance in the vagal center, in the ganglia of the heart or in the resistance offered by the myoneural junctions of the vagus? Or, do they mean a hypersensitivity of the vagus nerve? Furthermore, what brings about such a state? Is it due to a chemical substance elaborated by the disease or to some reflex factor that summates with the impulses coming from the carotid sinus region? In the latter case one should not consider it sensitization, but summation.

From a physiologic viewpoint, coronary disease meaning not merely coronary sclerosis but also coronary insufficiency, may explain a hyperactive cardioinhibitory carotid sinus reflex even in the authors' few cases. All physicians are familiar with the anginal syndrome induced by biliary tract disease in some patients, especially in the older age groups where coronary sclerosis is usually present. The authors themselves observed it in some of their cases. It is also now generally agreed that the anginal syndrome is due to acute coronary insufficiency caused by increased heart activity during effort or excitement, or by reflex angiospasm of the coronary vessels. It can therefore be readily understood how acute biliary tract disease may produce coronary angiospasm and resultant coronary insufficiency by impulses set up in the interconnecting vagosympathetic system of the abdominal organs and the heart and thus produce the anginal syndrome and a lowering of the resistance of the myoneural connections and of the ganglionic synapses of the vagus nerve in the heart.

It is interesting to find that all the authors' 18 patients who presented a positive carotid sinus cardioinhibitory reflex were over forty-one years of age, and most of them

over fifty, when coronary sclerosis detectable or not detectable by clinical or laboratory means is to be expected. The potentiality for an acute coronary insufficiency to develop in such cases under any provocative factor is always present.

It would be interesting to learn how many patients less than forty years of age exhibit the anginal syndrome and the hyperactive cardioinhibitory reflex in biliary tract disease. The fact must be appreciated, however, as I have brought out in my papers to which the authors refer, that the hyperactive cardioinhibitory carotid sinus reflex often occurs also in the absence of coronary disease, probably owing to a constitutional weakness in the synapses, which lowers their resistance.

The authors are wrong in their implication that I advocate the hyperactive cardioinhibitory carotid sinus reflex as the sole diagnostic factor in coronary disease. I suggested its use merely as corroborative evidence in patients who present clinical evidence suggestive of the presence of coronary disease. As such it is occasionally of greater value than the electrocardiogram, and is oftener positive.

Those who have had sufficient experience in electrocardiography know full well the limitations of the electrocardiogram as a diagnostic means.

LOUIS H. SIGLER, M.D.

255 Eastern Parkway
Brooklyn

POLITICAL RESPONSIBILITY OF PHYSICIANS

To the Editor Physicians are not properly represented in the legislative bodies of our cities, states and the Nation. Members of all other occupations, business and professional, are elected to office. Since physicians are not stepchildren they, likewise, should have adequate representation. I have often and in various ways, at Council and district meetings, tried to exhort, entreat and encourage physicians to make the sacrifice to become candidates for the Legislature. Indeed, at the recent primaries, after having failed to persuade a single physician to become a candidate, I was finally persuaded to seek the nomination in my district. Since compulsory state medicine is a possibility and since other important medical matters are scheduled to appear before the Legislature, Congress and the courts, it has become absolutely necessary that physicians should take part as members of the law-making bodies.

The National Physicians' Committee, whose work and activity were approved on June 9, 1942, by the House of Delegates of the American Medical Association, has exposed the existing conditions of medicine. We pay taxes and do millions of dollars' worth of careful and faithful work for the poor (and even for many who can afford to pay us, and do not), but no one is taking our part, we certainly do not merit the treatment we are receiving from politicians and the public.

Laymen seem to think that they must have lawyers in the law-making bodies. Of course, they are wrong, but it is up to us, who protect their health, to make them pay a little attention to our ideas. When an organization comes annually to the State House and wants to repeal the vaccination law and another wants to prevent us from using animals for experimentation (at one session, this was up for a second hearing), it is high time that we should protect the population and ourselves by having our own representation.

If compulsory state medicine is passed, the politicians will be in control and will order physicians around. The fine relations that exist between patients and physicians will disappear. Progress and advances in medicine will cease, and chaos will arise. Perhaps some physicians will benefit by this for they will work short hours and receive a fair salary.

Compulsory state medicine would take in hospitals, physicians, nurses, pharmacists and everything else that has to do with medicine. This would involve an expenditure of somewhere in the region of \$3,500,000,000 to \$5,000,000,000 (which would be controlled by politicians). Physicians must take a determined interest in this matter and definitely express an opinion. California has already defeated such a measure—physicians, hospitals, nurses and pharmacists must awake and act, not tomorrow but now.

Since the Massachusetts Medical Society has just started a plan that will eventually, I trust, take care of the complete cost of adequate medical care, there seems to be little excuse for compulsory state medicine. If we, as physicians, take heed at this time and pay attention to the advice of the American Medical Association and of the National Physicians' Committee to take our own part, we can benefit, and any proposed bill to inaugurate compulsory state medicine can be defeated.

HENRY M. LANDESMAN, M.D.

429 Marlborough Street
Boston

DEPRIVATION OF LICENSES

To the Editor: At a meeting of the Board of Registration in Medicine held October 14, the Board voted to revoke the license of Dr. William E. R. Basch, 183 Harvard Avenue, Allston, because of gross professional misconduct in the practice of his profession.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

To the Editor: At a meeting of the Board of Registration in Medicine held October 14, the Board voted to revoke the license of Dr. Earl Gordon Hersey, 12 Faxon Road, Quincy, because of gross professional misconduct in the practice of his profession as shown by his conviction in court.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

REPORT OF MEETING

WILLIAM HARVEY MEDICAL SOCIETY

The season's first meeting of the William Harvey Medical Society of Tufts College Medical School was held at the Beth Israel Hospital on September 25, with Dr. A. Warren Stearns presiding. The speaker of the evening was Dr. Alan Moritz, professor of legal medicine at the Harvard Medical School, and his subject was "Distinguishing Characteristics of Forensic Pathology."

In contrast to the ordinary hospital postmortem, the medicolegal autopsy is usually of immediate importance to some living being; in fact, it may determine the life or death of such a person. It may also serve to place great financial liability. The hospital postmortem, on the other

hand, usually has only educational value. The medicolegal autopsy, furthermore, is frequently contested hotly by one or several "experts," whereas when the hospital pathologist gives his opinion it is usually considered final.

One of the problems of forensic pathology not ordinarily met by the hospital pathologist has to do with identification. Strange as it may seem, there are an astounding number of missing persons at any one time, and the lack of interest on the part of relatives and friends may be a great handicap. Often nothing but a skeleton is found, and even bones of bears and the primates have sometimes been confused with those of human beings. The roentgenologist is often of inestimable value in determining the identity of an unknown skeleton. Often age can be fairly accurately computed from the character of the epiphyses. The height may be estimated by Pearson's formula, even though only the humerus or femur is available. Sex may usually be recognized from the clothing and, failing that, from the character of the pelvis and other bones. The approximate weight of the individual is somewhat more of a problem, but can sometimes be estimated from stature and clothing.

Information regarding the time of death is frequently of inestimable value in ruling out certain persons in a suspected crime. One cannot always accurately determine the exact time of demise, but it is often sufficient to place the time within a few days or even within a certain month. Specimens taken from different areas of injury may confirm the suspicion that the wounds are of different ages, that is, that some were inflicted an appreciable time before death. A botanist may aid by determining how long a plant or bush has been crushed beneath a body, and an entomologist may add some information by judging the age of the eggs of vermin found devouring a body. Either may place time of death within a two-week period and thus incriminate or free a suspected person.

The medicolegal pathologist must develop a suspicious mind and never be satisfied with the plausible cause of death. An example was cited where a man known to have coronary disease was found dead with no evidence of external violence. A complete autopsy, however, revealed a recent large subdural hematoma underlying a bruise of the scalp, which had been covered by his bushy hair. To determine whether or not a death is accidental is often of extreme monetary importance to the relatives of the deceased. There are many places in the body where external violence may be easily missed or where the latent period between injury and death may be long enough to allow healing of the external wound. On the other hand, death from coronary infarct or cerebral accident may be complicated by the finding of signs of external violence that are, in reality, secondary to a fall.

A knowledge of the fundamentals of firearms is almost a prerequisite for a good forensic pathologist, since it is often his duty alone to call attention to some irregularity in the death of a person who has been shot. Such acuity may result in a decision that the shooting was accidental rather than a homicide. The pathologist may be the only one responsible for collecting bullets or other material that may serve to determine the origin of the ammunition and the gun. Ballistics experts are valuable in identifying the gun in question. The character of the combustion residue on the hand or clothing of the deceased may be an important clue in a question of suicide or homicide, and the amount and distribution of powder around the wounds of entrance are of great value.

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CHOLANGIOGRAPHIC ARTIFACTS RESEMBLING COMMON-DUCT STONES

HOWARD M. CLUTE, M.D.* AND LIEUTENANT KNOWLES B. LAWRENCE, M.C., A.U.S.†

BOSTON

WHENEVER the common bile duct is opened for exploration during the course of operations for gallstones, it is drained with a T tube. In every case, the problem of when to remove this tube must be settled on certain objective facts, which in their entirety show that the common bile duct is patent and contains no residual or over-looked calculi.

For many years, surgeons depended on the clinical findings following the clamping of the T tube for the decision that the common duct was free and clear of stones. Thus, on the fifth or sixth postoperative day, the T tube was clamped off and the results were carefully observed. If no pain or colic occurred, and if no bile drained around the sinus tract, one was relatively certain that the common bile duct was patent. Usually, the tube was clamped off for six or eight days to prove this point, and then, on the twelfth postoperative day, it was removed.

Unfortunately, it is true that a stone may be left in the common duct and yet may give no clinical evidence of its presence during the time the T tube is clamped off. To avoid this trouble, visualization of the common bile duct by the injection of a radiopaque substance through the T tube and the taking of quick x-ray films^{1, 2} has been developed in recent years as a means of gaining further objective information regarding the patency of the common duct. These post-operative cholangiograms have proved to be highly reliable, and on our service, we routinely visualize all common ducts after T tube drainage before removing the tube.

Fluoroscopic studies and roentgenograms of the common bile duct may demonstrate the following findings.

Normal.

Filling or partial filling of a normal biliary-duct system.

Passage of the opaque medium through the ampulla of Vater, which either is patent at the time of injection or becomes so shortly thereafter by relaxation of its muscular sphincter.

Abnormal

Dilatation of the biliary-duct system

Presence of a foreign body, notably a residual calculus, shown by positive or negative shadows

Failure of the opaque medium to enter the duodenum owing to an obstructing calculus or a persistent spasm of the sphincter of Oddi.

We have believed that a filling defect in the common bile duct as shown in cholangiograms meant that a stone had been left behind, and subsequent events have generally confirmed this belief. This has necessitated the use of the Best-Hicken³ regime to relax the sphincter of Oddi in a few cases. In others, we have successfully followed Pribram's⁴ suggestion for dissolving residual cholesterol stones by washing out the common duct with ether. In only the rarest case has reoperation for these stones been necessary in our experience in recent years.

In four recent postoperative cholangiograms, however, we found a filling defect in the common duct close to the lower end of the T tube that was suggestive of a residual stone but was demonstrated, on further study in each case, to be an artifact. In none of these cases had stones been present in the duct at operation. This fact first aroused our suspicion that the x-ray picture might be due

*Professor of surgery, Boston University School of Medicine; surgeon in chief, Massachusetts Memorial Hospitals

†Assistant in surgery Boston University School of Medicine and assistant surgeon, Massachusetts Memorial Hospitals (on leave of absence)

to something other than stone. Hicken et al.⁵ mention cholangiographic filling defects in the common duct, apparently due to floating clots and air bubbles, although these were different from those we have noted.

A clot of old blood, bile and mucus clinging to the lower end of the T tube was found to be the cause of the filling defect in 3 cases, as demon-

If one is convinced that the filling defect is due to such an artifact, because of the appearance described, removal of the tube without further procedure is probably justified. If the tube is removed gently and without rotation, the clot or part of it may still be clinging to its lower end, when brought into view. The safer procedure, however, is to irrigate the T tube periodically until

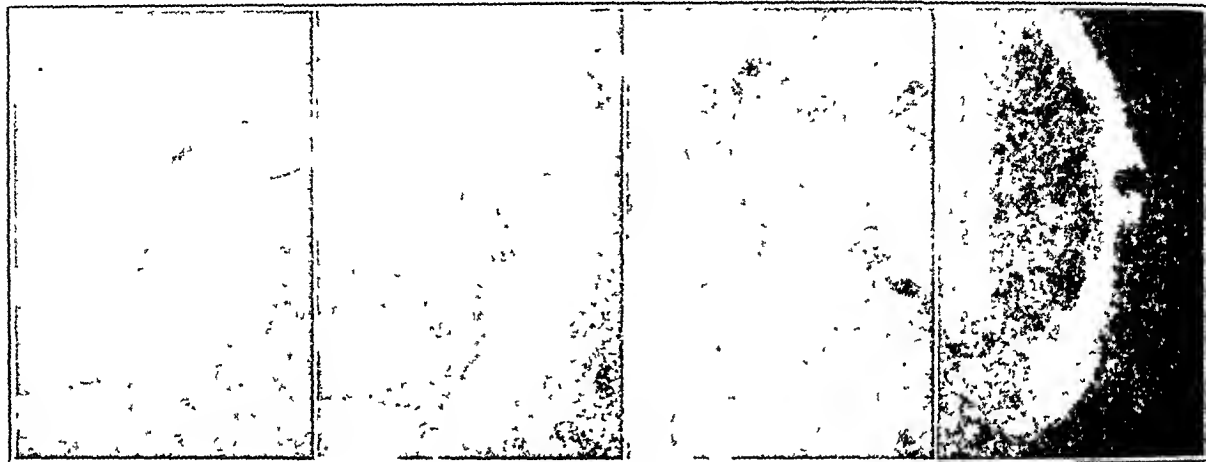


FIGURE 1. Case 1: Cholangiograms on Various Days.

This patient had a postoperative blood clot in the common duct. Note the variations in the shapes of the filling defect from day to day, with no change in its relation to the end of the T tube. There is a long streak-like filling defect in the first film, which probably represents a mucous streamer from the clot. Note the reduction in the size of the defect.

strated on removal of the tubes. This was confirmed by the smooth recovery of the patients. In 1 of these cases, repeated cholangiograms demonstrated a diminution in the size of the filling defect over several days, probably as a result of the mechanical irrigation of the tube. The clot did not obstruct the flow of bile in any of these cases, and colic was not produced.

The features of this type of cholangiographic artifact that helped in the differentiation of the adherent clot from actual stone, or from other solid foreign bodies in the common duct, were as follows: the filling defect appeared in direct, or nearly direct, contact with the lower end of the T tube; the defect changed in shape in serial roentgenograms because of the malleability of the soft clot by action of the bile current, of the injected radiopaque medium or of the local-duct contraction or relaxation; close examination of the x-ray films revealed streaklike defects extending from the principal filling defect several centimeters distally in the duct—this appearance was probably produced by streamers attached to the main clot; irrigation through the T tube and the injection of the opaque medium apparently washed part or all of the clot from its attachment to the tube, and thus changed the appearance of the filling defect in subsequent films.

repeated cholangiograms no longer demonstrate the filling defect, or until it is apparent that the defect is not caused by a retained common-duct stone.

The following is a typical case.

CASE 1. C. W., a 58-year-old man, had suffered with attacks of biliary colic for a year. Cholecystograms showed gallstones. One month before admission, coincident with such an attack, the patient became jaundiced.

Operation was performed on January 19, 1942. A chronically inflamed gall bladder containing several small mulberry-type stones was removed. The common duct, which was three times the normal diameter, with inflamed and thickened walls, was explored and found empty, and the sphincter of Oddi was apparently patent. A T tube was sutured into the duct for drainage.

The postoperative course was uneventful. The T tube was clamped off on the 5th postoperative day. On the 10th day, a cholangiogram was done by injection of lipiodol through this tube. X-ray study demonstrated a rounded defect in the common duct, just beyond the lower end of the T tube (Fig. 1). The lipiodol seemed to have flowed around it readily enough, and passed into the duodenum after a short delay. On re-examination 3 days later, the defect, although still in the same position, was much smaller. The T tube was irrigated with physiologic saline solution. In a third cholangiogram, after another 48 hours, however, the defect showed little further change in size. It was then considered safe to remove the T tube because of the cholangiographic appearances described above—that is, the variation in shape of the filling defect,

the diminution in its size after simple irrigations, the nearly constant positional relation to the lower end of the T tube and the streamer defect noted in the first cholangiogram. On removal of the T tube, directly after the

seemed to show further air shadows surrounding the upper arm of the T tube. Two days later, another cholangiogram was made and more negative shadows were found. The previous shadows were absent. At each injection,



FIGURE 2 Case 2 Cholangiograms

The air bubbles in these films resemble common duct stones. Note the air around the arms of the tube, the changing size and symmetry of the bubbles and the rapid and ready emptying of lipiodol into the duodenum.

third cholangiogram, a soft bile stained clot of blood and mucus was found clinging to the lower arm of the tube at its tip. This measured about 5 mm in greatest diameter. The sinus drained bile for about 36 hours, and then stopped. The patient has remained asymptomatic since that time.

Air bubbles may be present in the common duct and may give a shadow very suggestive of a smooth, oval, residual stone. These air bubbles are said by x-ray men to be the commonest artifact seen in postoperative choledochograms, but this has not been our experience. We have recently had a case, however, in which we found it difficult to convince ourselves that the stone-like shadows seen following postoperative common duct injections were air bubbles and not stones.

CASE 2. At operation, the gall bladder was found much thickened and chronically inflamed. It contained one large stone, which was removed, exploration of the common duct revealed no stones. On the 5th or 6th postoperative day, the T tube was clamped off, with no untoward results. On the 12th day, cholangiograms (Fig 2) were made. In these x-ray films, negative shadows just below the lower arm of the T tube were noted. Close inspection

it was noted that the lipiodol flowed readily and freely into the duodenum. The T tube was removed after the second x-ray examination, and bile drainage from the sinus ceased in a few hours. Recovery was uneventful.

In this case, it became apparent that the negative common duct shadows were air bubbles and not stones because of their change in size and position and because of the other evidences of air around the arms of the T tube. In this and similar cases, however, it is apparent that repeated cholangiograms should be made to prove that the shadows in the common duct are not stones but artifacts.

SUMMARY

Artifacts simulating common bile duct calculi after choledochostomy and observed in postoperative cholangiograms are described.

The filling defect in 3 such cases was due to a clot of blood, bile and mucus clinging to the lower end of the choledochostomy tube. In a fourth case, the artifact was caused by air surrounding the T tube.

X-ray films demonstrating these cholangiographic artifacts are reproduced and comments on their proper interpretation are made.

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HEMOLYTIC STREPTOCOCCUS BACTEREMIA*

A Report of Thirteen Cases with Special Reference to the Serologic Groups of the Etiologic Organisms

LOWELL A. RANTZ, M.D.,† AND WILLIAM M. M. KIRBY, M.D.‡

SAN FRANCISCO

THE study of hemolytic streptococcus disease has been greatly enhanced by the application of the serologic methods of classification devised by Lancefield.¹ Extensive observations have shown that organisms of Group A are responsible for nearly all the infections of the respiratory tract, such as scarlet fever, tonsillitis, otitis media and pneumonia.^{2,3} Organisms of this group are also responsible for many infections of other organs, particularly the skin and female genitalia. A recent study in this clinic, however, demonstrated that only 25 per cent of the hemolytic streptococci isolated from sources other than the respiratory tract were members of Group A.⁴

It is important to evaluate the nature and severity of the infections caused by the streptococci of these various groups, since their course and response to sulfonamide and other therapy may well be different. For example, a recent study of Group D infections showed that the sulfonamides were without effect,⁵ a conclusion for which there is adequate experimental evidence.⁶

Because invasion of the blood by the hemolytic streptococcus occurs only in conjunction with severe infectious processes,^{7,8} the presence of bacteremia may be used as an indication of the frequency with which members of the various Lancefield groups are responsible for serious disease. An earlier comprehensive study of this problem^{2,9} revealed that 90 per cent of strains of hemolytic streptococci recovered from the blood were members of Group A, but 85 per cent of the cases studied were those of respiratory infection.

Observations in several clinics^{10,11} demonstrate that organisms of Groups B, C and G are responsible for 10 to 25 per cent of all cases of hemolytic streptococcus puerperal infection, and that

approximately 25 per cent of the cases of puerperal septicemia are associated with members of these groups. The prognosis in these cases has been poor, since the disease is severe and endocarditis frequently present.

The purpose of this paper is to emphasize further the fact that hemolytic streptococci of groups other than Group A are frequently the cause of serious infections in man, by presenting a study of 13 consecutive cases of hemolytic streptococcus bacteremia observed in this clinic, in only 6 of which Group A organisms were the etiologic agents. The results of sulfonamide therapy in several of these cases will be described.

It should be emphasized that this study was conducted in a community in which hemolytic streptococcus infections of the respiratory tract are mild and relatively uncommon; that no contagious disease ward is associated with the clinic; and that the majority of the patients are admitted for diagnostic study, elective surgery or normal labor. For these reasons, the character of hemolytic streptococcus infections observed is different from that described in other centers.

The distribution of the organisms isolated from the blood among the various Lancefield groups is as follows: Group A, 6 cases; Group B, 4 cases; and Groups C, D and G, 1 case each. Organisms were isolated only from the heart's blood at autopsy in 4 cases (1 case of Group A, 2 cases of Group B and the case of Group G infection); no ante-mortem blood cultures having been performed.

CLINICAL DATA

Group A

Hemolytic streptococci of Group A were isolated from the blood of 6 patients. These cases, similar to those observed and described previously,⁷ need not be considered in detail.

*From the Department of Medicine, Stanford University School of Medicine, San Francisco.

†Assistant professor of medicine, Stanford University School of Medicine.

‡Assistant resident in medicine, Stanford University Hospitals.

Four patients were treated with sulfonamides. Recovery occurred in a case of pneumonia and empyema in a young woman treated with sulfapyridine, and in another case of pneumonia, complicated by suppurative arthritis in a seventy-year-old man suffering from chronic lymphatic leukemia, who was treated with sulfadiazine. Two patients who received chemotherapy died. One was a young girl with otitis media, osteomyelitis of the temporal bone and meningitis; the other was an elderly man in whom bacteremia complicated an infected ulcer of the leg, associated with congenital hemolytic jaundice. No clinical data were available on one of the 2 remaining cases. The last was an example of acute hemolytic streptococcus peritonitis, which followed an exploratory laparotomy in an elderly man whose liver was discovered to contain metastases from a carcinoma of the stomach. Chemotherapy was not instituted, and the patient died within five days of the onset of symptoms of infection.

Thus, 3 cases of Group A bacteremia associated with disease of the respiratory tract were observed. Recovery occurred in 2 cases in which the primary disease was in the lungs. Meningitis, complicating otitis media, resulted in death in the third. Infections of the skin and of the peritoneal cavity in 2 chronically ill men were followed by death.

This small group of cases does not permit an evaluation of the most effective sulfonamide drug for use in the treatment of serious infections caused by Group A streptococci. The dramatic recovery of an old man, debilitated by chronic lymphatic leukemia and suffering from pneumonia and suppurative arthritis, suggests that sulfadiazine will be found to be an unusually effective agent for the treatment of these infections.

Group B

Four cases of invasion of the blood by Group B hemolytic streptococci were studied. In 1 the organisms were recovered from the heart's blood at autopsy in a man who had died of carcinoma of the lung, and were probably terminal invaders. The other 3 cases are of special interest and are presented in greater detail.

CASE 1. An elderly male diabetic patient entered the hospital with a history of diabetes mellitus for 15 years and a painful left 5th toe for 2 weeks. X-ray evidence of osteomyelitis of the phalanges was present, and the toe was amputated. Three weeks later an abscess of the left foot was drained, and cultures of the purulent exudate showed *Staphylococcus aureus* and hemolytic streptococci, which were not grouped serologically. A guillotine amputation of the left leg in the thigh was performed because osteomyelitis of the metatarsal was discovered to exist. Infection of the stump followed, and the patient died 1 week after operation. Group B streptococci were recovered from

the heart's blood at autopsy. Sulfonamides were never administered.

CASE 2. A laminectomy was performed, and a meningioma was removed from the midthoracic region of a middle-aged woman. Six days after the operation she developed a stiff neck, a positive Kernig's sign and fever. The spinal fluid was purulent, and Group B hemolytic streptococci were recovered from it and from the circulating blood.

Sulfapyridine was administered 24 hours later, at which time the blood culture was sterile and the temperature was lower. The patient recovered uneventfully after 3 days of chemotherapy.

CASE 3. A 30-year-old woman was delivered at term after a 24-hour labor complicated by a transverse presentation of the fetus. The temperature rose within 24 hours to 40°C, and Group B streptococci were isolated from the interior of the uterus. Six grams of sulfanilamide was administered daily for the following 9 days, during which time she remained desperately ill. The first blood culture, obtained on the 8th post partum day, showed two colonies of hemolytic Group B streptococci per cubic centimeter. The sulfanilamide was immediately replaced by sulfapyridine, and within 49 hours the temperature was normal and the patient made an uneventful recovery.

Thus Group B hemolytic streptococcus bacteremia was observed in 4 cases. In 1 the organisms invaded the blood as a terminal event of another fatal illness. The recovery of Group B streptococci from the heart's blood of a patient with osteomyelitis, in whom cultures of the purulent material obtained from the region of the bone also revealed hemolytic streptococci, suggests that these organisms may have been etiologically related to the suppurative process that eventually proved fatal. It is unfortunate that the streptococci recovered from the local lesion were not classified serologically.

A patient with postoperative Group B streptococcal meningitis and bacteremia recovered following the administration of sulfapyridine. Because the blood had already become sterile and the temperature lower when the drug was first exhibited, it is quite possible that recovery would have occurred in the absence of chemotherapy. This case has been described elsewhere,¹² and it was proposed that infection of the meninges with streptococci not of Group A may account for certain spontaneous recoveries from hemolytic streptococcus meningitis.

The last case in this group is of great interest. Puerperal sepsis caused by Group B streptococci was not associated with endocarditis or the development of local suppuration described by others.¹³ Furthermore, the patient recovered following sulfonamide therapy. Most important, however, is the fact that sulfanilamide failed to exert a beneficial effect on the course of the disease, and the blood was not sterilized, whereas the admin-

istration of sulfapyridine was followed by immediate recovery. This result suggests that sulfanilamide should not be used in the treatment of infections due to Group B streptococci. Sulfapyridine is apparently an effective agent, and it is reasonable to hope that sulfathiazole and sulfadiazine may also be valuable therapeutic chemicals for use in these cases.

Group C

Group C hemolytic streptococci were isolated from the circulating blood of an old man with an aplastic anemia who developed chills and fever following a skin infection. Treatment with sulfadiazine resulted in prompt recovery, even though less than 500 granulocytes per cubic millimeter were demonstrable in his blood. He died several months later of inadequately treated colon bacillus bacteremia. This individual developed antistreptolysins and antifibrinolysins indistinguishable from those that are present in the blood following recovery from infections with Group A streptococci.

The striking results of treatment indicate that sulfadiazine is an exceedingly effective chemotherapeutic agent for use in infections due to Group C streptococci.

Group D

Group D hemolytic streptococci were recovered from the blood of an old man whose primary infection was in the kidney. Ten days before entry to the hospital he had developed chills and fever. Seven days later sulfapyridine was administered, followed by the development of complete anuria. The kidney pelvis were lavaged for the purpose of dissolving the probable sulfapyridine calculi shortly after admission to the hospital. The urine obtained from the catheters contained innumerable cells and hemolytic Group D streptococci. Blood cultures obtained after the cystoscopy was completed, showed a growth of similar streptococci. No further sulfonamides were administered. The patient recovered uneventfully from the acute episode, but bacteriuria and pyuria persisted.

In summary, this was an example of Group D streptococcus pyelonephritis, complicated by the formation of sulfapyridine calculi and anuria. Bacteremia may have occurred as a result of instrumentation of the urinary passages.

Hemolytic and nonhemolytic Group D streptococci are well known. Together they constitute a division of the streptococci known as the enterococci, of which *Streptococcus faecalis* is the typical nonhemolytic variety. All these organisms are exceedingly resistant to the bacteriostatic action of the sulfonamides in vitro, and in a recent review of a large group of infections caused by them, it

was demonstrated that the sulfonamide drugs do not favorably affect the clinical course of Group D infections.⁵ Cases of nonhemolytic enterococcus bacteremia were presented in that report.

DISCUSSION

It has been well established that primary infection of the respiratory passages by hemolytic streptococci is nearly always caused by members of Lancefield Group A, but recent observations have demonstrated that these organisms are much less often the etiologic agents in infections of other organs. The frequency with which streptococci of the various groups may be isolated from the circulating blood of patients in whom infection is present may be used as an index of the severity of the disease processes caused by each. Previous studies show that hemolytic streptococci isolated from the blood in cases of scarlet fever, tonsillitis, otitis media and their complications will almost invariably be Group A strains, but that this will not be the case if the primary infection is located in the female genitalia, the skin, the kidney or the abdominal cavity.

Thirteen consecutive examples of hemolytic streptococcus bacteremia have been presented to emphasize these facts. No clinical data were available in 1 and terminal invasion of the blood occurred in 2. Three were cases of primary infection of the respiratory passages, and all were caused by Group A streptococci. The remaining 7 were examples of infection of the skin or kidney or were the result of surgical procedures. Strains of hemolytic streptococci of Groups B, C and D were the etiologic agents in 5 of these cases.

The results of sulfonamide therapy were of interest. Two Group A patients recovered and 2 died. The favorable effect of sulfadiazine in 1 case of Group A pneumonia and suppurative arthritis complicating chronic lymphatic leukemia was most remarkable. Two cases of Group B infection were treated with sulfapyridine. In one, postoperative meningitis appeared to be subsiding at the time therapy was instituted. In the other, a case of puerperal sepsis, sulfanilamide was without effect, but a change to sulfapyridine was followed by prompt recovery. One patient with Group C infection recovered after the exhibition of sulfadiazine, in spite of the presence of an aplastic anemia with agranulocytosis.

In a previous study,⁵ it was demonstrated that the drugs of the sulfonamide group were without effect in infections caused by Group D streptococci. Suggestive evidence is presented here that sulfanilamide may not be of value in serious Group B infections. It is apparent that the determination of the serologic group of a streptococcus recovered

from the blood or other clinical materials, particularly if the primary infectious process does not lie within the respiratory passages, is of definite importance. At the present time, sulfanilamide is the most widely used chemical for the treatment of hemolytic streptococcus infections, but may not be the drug of choice in certain cases. In others, the presence of Group D organisms may suggest that sulfonamides be withheld, or may explain their therapeutic failure.

The accumulation of further observations, similar to those described here, will also contribute to a more complete understanding of the nature, course and prognosis of serious disease caused by the less common groups of hemolytic streptococci.

SUMMARY

Streptococci of Lancefield Group A were responsible for only 6 of 13 cases of hemolytic streptococcus bacteremia.

Organisms of Group A are almost invariably the cause of serious primary hemolytic streptococcus infections of the respiratory tract.

Severe infections of other organs are frequently due to streptococci of other groups, particularly Groups B, C, D and G.

The importance of serologic classification of the hemolytic streptococci in relation to certain aspects of sulfonamide therapy is discussed.

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PHONOCARDIOGRAPHIC STUDIES IN A CASE OF PAROXYSMAL TACHYCARDIA

HENRY WEYLER, M.D.,* AND CECIL C. DUSTIN, M.D.†

PROVIDENCE, RHODE ISLAND

CLINICAL descriptions of the heart sounds at the onset of paroxysmal auricular tachycardia are vague. They are usually described as sharper and louder than normal or as having a clicking quality. The phonocardiograms that are to be described in this paper are of particular interest because they show changes in sound at the onset of auricular tachycardia and present a clearer description of the events taking place.

In order to interpret phonocardiograms it is necessary to distinguish between the stethoscopic and logarithmic registration of sound. As pointed out by Rappaport,^{1,2} the stethoscopic method records sounds as they are presented to the ears of the observer by an average acoustic stethoscope, modified by the instrument but not modified by human hearing. Sounds of low frequency are best recorded by this method. The logarithmic method,

on the other hand, modifies the sounds of the heart exactly as does the combination of the average acoustic stethoscope plus average hearing. In the following description of phonocardiograms it is to be noted that comparative measurements of loudness will be made on the logarithmic tracings, the sounds being similar to those heard by a person with average hearing using the ordinary acoustic stethoscope.

In the case being presented the stethoscopic phonocardiograms (Fig. 1) show during the normal heart beat a definite auricular sound, which occurs between the P and Q waves in the electrocardiogram. The first sound is distinct and commences with the R wave. The second sound starts at the end of the T wave. There is a third heart sound and evidence of a midsystolic murmur. When paroxysmal tachycardia sets in, the sounds change. The auricular sound gradually increases in intensity during the first few beats. The first sound, on the other hand, in most of the runs of tachycardia immediately shows a marked

*Assistant visiting physician, Rhode Island Hospital, assistant cardiologist Providence Lying in Hospital.

†Visiting physician Rhode Island Hospital cardiologist Providence Lying in Hospital.

increase in intensity and remains at about the same level throughout the tachycardia, becoming at times slightly higher after the first few beats.

increase in intensity with the onset of the tachycardia. At the same time the auricular sound gradually increases in intensity and duration, thus

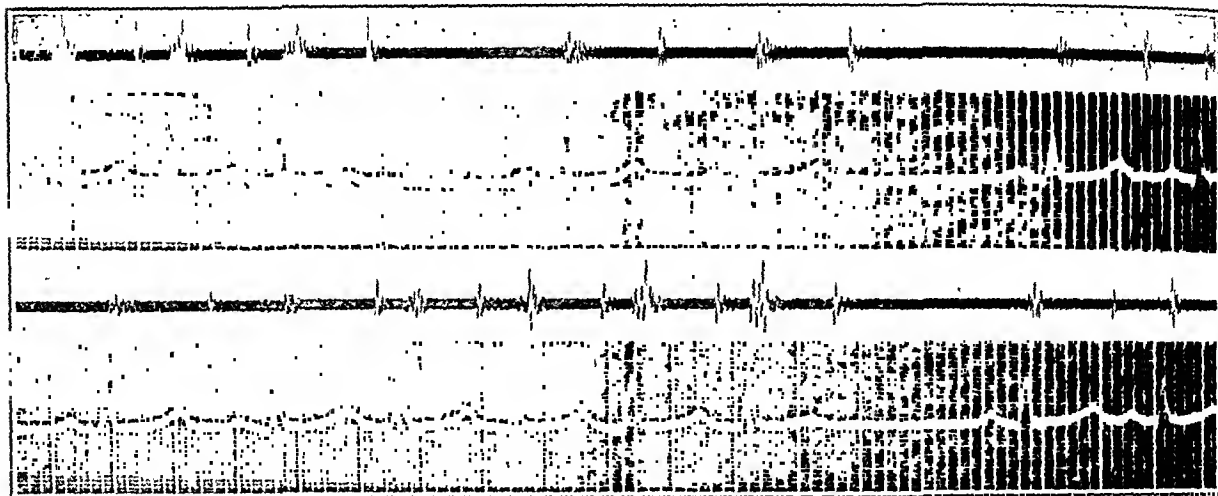


FIGURE 1. Phonocardiograms by the Logarithmic and Stethoscopic Methods.

The upper record was made by the logarithmic method. It shows the end of a run of auricular tachycardia, followed by two slow beats, the first of which is considered normal for this patient. Note the absence of auricular sounds during the tachycardia.

The lower record was made by the stethoscopic method. It shows the onset of auricular tachycardia. There is a gradual increase in intensity of the auricular and first heart sounds. (Most of the runs of tachycardia in this patient showed a more abrupt increase in loudness of the first heart sound at the onset of tachycardia.) The auricular sounds in this case were below human audibility.

Both diastole and systole become shorter—diastole more so than systole. The second sound also becoming part of the first sound after the first, second, third or fourth beat.

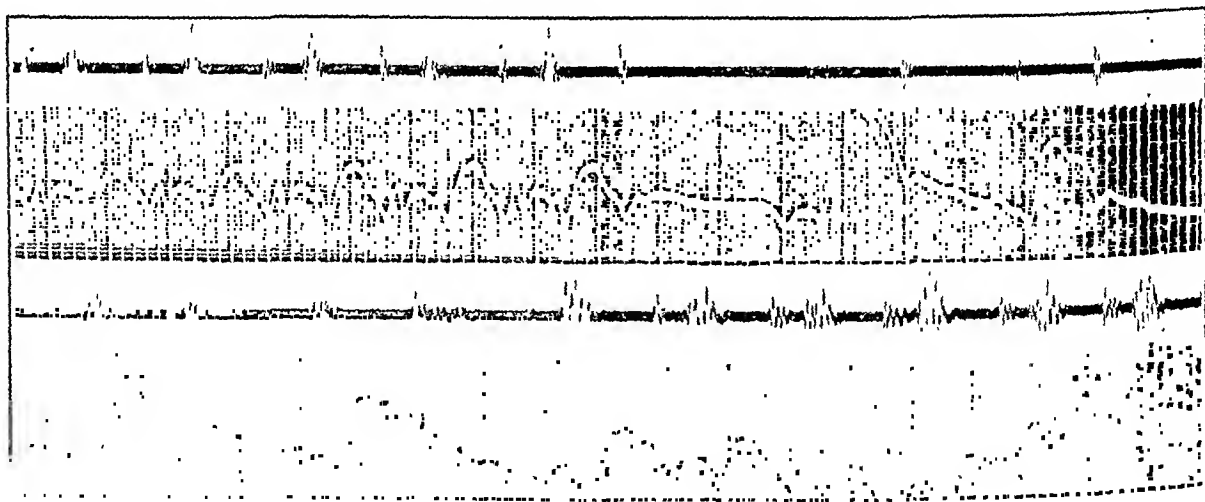


FIGURE 2. Phonocardiograms and Jugular Tracings.

The upper record was made by the logarithmic method. It shows a run of tachycardia just after onset, followed by two slow beats. The jugular tracing shows a carotid effect. All sound tracings were made from the region of the apex of the heart.

The lower record was made by the stethoscopic method. It shows the abrupt onset of the tachycardia after two slow beats.

increases in intensity but not with the same increment as the first sound. It is to be pointed out again that the first sound attains a marked

Phonocardiograms registered by the logarithmic method during the normal slow beats show no auricular sound in most of the tracings. Occa-

sionally an auricular beat of very low intensity is seen. This indicates that the auricular sound recorded by the stethoscopic method is for the most

than it is during the normal slow beats. Because of variations in the normal heart sounds in this case, one cannot expect to find a constant ratio

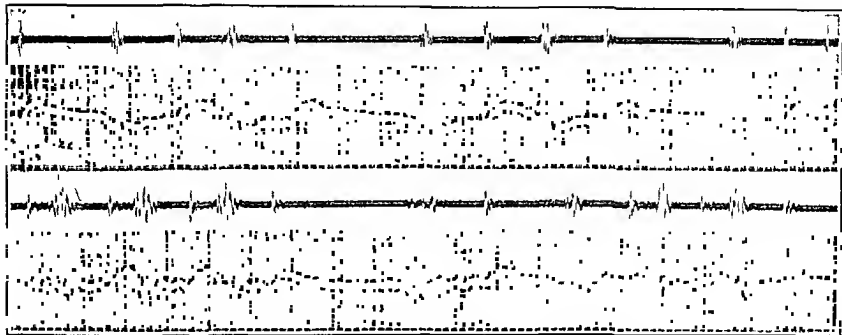


FIGURE 3 Phonocardiograms and Apex Cardiograms (Linear Tracings)

The upper record was made by the logarithmic method, and the lower by the stethoscopic method. Vibrations consistent with a systolic murmur are present in both records. The stethoscopic phonocardiogram shows the end of a run of tachycardia and the onset of another run.

part below human audibility so that any increase in loudness of the first sound at the onset of tachycardia is not due to summation.

The first sound is distinct and commences with the R wave and is, in turn, followed by a decreascent systolic murmur. The second sound occurs at the end of the T wave. When the long pauses occur, the third heart sound is not present because it is below human audibility. When tachycardia sets in, there is an abrupt increase in intensity of the first sound with a slight increase in the second sound. Still, no auricular sound is recorded. There is a remarkable uniformity in the loudness of the first sound throughout the paroxysmal tachycardia. This also holds true for the second sound. In contrast, when the first sound of one normal slow beat is compared with the first sound of another normal slow beat there is considerable variation in loudness.

The second sound shows less variation in these records. Any changes in ratio between the intensity of the normal slow beat and the intensity of the tachycardia are due to variations in the loudness of the slow beat rather than to the more fixed loudness of the tachycardia. The first sound during tachycardia is from 2.1 to 4.5 times louder than it is during the normal slow beats. Similarly, the second sound is from 0.10 to 0.13 times louder

between the normal heart sounds and the abnormal sounds found in the tachycardia.

The phonocardiograms taken with the jugular cardiograms (Fig. 2) and the apex cardiograms or linear phonocardiograms (Fig. 3) corroborate the above findings.

SUMMARY

Phonocardiographic studies were made in a case of auricular tachycardia. Logarithmic phonocardiograms show an abrupt increase in intensity of the first sound, 2.1 to 4.5 times louder than the first sound in the normal slow beats. The second sound is only slightly increased in intensity, being 0.10 to 0.13 times louder than the normal slow beats. Stethoscopic registrations show a gradual increase in the auricular sound during the first few beats. In the case reported, the auricular sound is, for the most part, below human audibility.

These findings suggest that loudness of the first sound at the onset of tachycardia is not entirely due to summation.

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CLINICAL NOTE

ADRENALIN BASE SUSPENDED IN AN AQUEOUS SOLUTION OF SODIUM THIOLYCOLATE IN THE TREATMENT OF ASTHMA*

CAPTAIN HYMAN L. NATERMAN, M.C., A.U.S.†
BOSTON

KEENEY¹ has shown that adrenalin base suspended in oil has a prolonged effect and is beneficial in the treatment of some cases of persistent asthma. My² experience with oil preparations has suggested that it was the insolubility of adrenalin base in tissue fluids rather than the use of oil as a vehicle that was responsible for their prolonged action. Moreover, repeated subcutaneous injections of oil cause induration in the skin. Therefore, a method of preparing stable suspensions of adrenalin base in water was sought. Adrenalin base suspended in water oxidizes rapidly. Although reducing agents prevent this oxidation, acid-reducing agents are not suitable because they convert the insoluble base adrenalin into the soluble acid salt. Accordingly, a reducing agent effective at a pH of 7.0 or higher is necessary; sodium thiolglycolate meets these requirements. The method of preparation and the results observed in the treatment of 5 asthma patients with adrenalin base suspended in a solution of sodium thiolglycolate in water are presented.

Adrenalin base‡ and suprarenin base§ were used. The most satisfactory method of preparation was to dissolve sodium thiolglycolate|| in distilled water, and to neutralize this with disodium

phosphate. Glycerin and chlorbutanol were added. The final proportions were sodium thiolglycolate 2 per cent, glycerin 10 per cent and chlorbutanol 0.5 per cent. The solution was sterilized by autoclaving or, preferably, by Berkefeld filtration. Adrenalin base was then added to make a suspension containing 2 to 4 mg. per cubic centimeter. The suspensions were bottled in sterile rubber-capped vials of 20 to 50 cc. Such suspensions frequently showed no evidence of oxidation for periods up to fifteen months, although in some lots changes in color suggestive of slight oxidation occurred. However, these slightly oxidized preparations lost no measurable amount of their potency.

Injections were self administered subcutaneously by the patients. After the vial had been shaken to disperse the adrenalin evenly, the required dose was taken out. The doses varied from 1 to 4 mg. Injections were given in some cases prophylactically to prevent attacks, and in others therapeutically to relieve attacks. They have been taken one to five times a day for periods as long as two years by the patients. The local reactions have been similar to those produced by adrenalin solution. General reactions have sometimes occurred, but usually three or more times the tolerated amount of soluble adrenalin may be given with no general adrenalin reaction. The intervals between attacks are prolonged and breathing is more nearly normal when adrenalin base suspended in water is used rather than adrenalin solution.

Adrenalin suspended in water seems to be as effective as, and in some cases more effective than, adrenalin suspended in oil. The easier administration and milder local reactions of adrenalin suspended in water are advantages over the oil preparation.

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*From the Department of Allergy, Beth Israel Hospital, Boston.

†Assistant in medicine, Harvard Medical School and Tufts College Medical School; associate visiting physician and associate in bacteriology and allergy, Department of Pathology, Beth Israel Hospital (on leave of absence).

‡Kindly furnished by Parke, Davis and Company, Detroit, Michigan.

§Kindly furnished by the Winthrop Chemical Company, New York City.

||Obtained from the Baltimore Chemical Company, Baltimore, Maryland, and later from the Eastman Kodak Company, Rochester, New York.

MEDICAL PROGRESS

ORTHOPEDIC SURGERY

GEORGE W. VAN GORDER, M.D.*

BOSTON

POLIO MYELITIS

ALTHOUGH the Kenny concept and treatment of infantile paralysis has been well described in a previous progress report by Watkins,¹ it is of sufficient importance to mention again, since it is one of the most outstanding advances in orthopedic surgery, as well as being a great contribution to the field of physical therapy. The usual conception that poliomyelitis produces simply flaccid paralysis is not tenable if one accepts the ideas of Sister Kenny, for she has proved that the major symptoms early in the disease are not so much flaccid paralysis as they are "muscular spasm," "inco-ordination" and "mental alienation."

The Kenny method of overcoming muscle spasm, tenderness and hyperirritability by means of the early application of hot packs instead of by immobilization in splints has done much to eliminate stiff joints, muscle contractures, spinal curvatures attributable to contractures and atrophy from disuse. Moreover, this new form of therapy followed by her system of muscle re-education has yielded functional results equal or superior to those of any other method.

FRACTURES AND DISLOCATIONS

Operative fixation of fractures of the clavicle by means of a Kirschner wire has been the subject of much discussion since Murray² wrote his original paper on the subject two years ago. In Murray's hands, these fractures seem to do extremely well, but the procedure requires considerable experience and the technic is more difficult than it appears to be from the author's description, which follows:

When a satisfactory reduction has been obtained a quarter inch [0.6 cm.] incision is made one inch [2.5 cm.] from the inner end of the clavicle. Through this, a hole, a quarter of an inch [0.6 cm.] in diameter, is drilled in the thin cortex. The direction of the drill is gradually changed from the perpendicular until it points toward the central cylinder. Through this hole a medium sized Kirschner wire is passed. If it is started in the right direction it always traverses the central cylinder and passes across the fracture line into the distal fragment, provided the reduction has been satisfactory. The clavicle immediately

becomes stable, and the arm, shoulder, and clavicle can be moved about quite freely without any displacement of the fragments. The wire is cut short and a small dressing is applied over the incision. If for some reason it is to be removed later on, this can be done through a very small incision under local anesthesia. No other fixation except a sling is required, and the patient is quite comfortable.

Several infections and one death are known to me to be the result of this method of treatment, and since open reduction is so seldom indicated in fractures of the clavicle, it seems questionable to adopt the procedure for routine use. However, in selected cases where conservative measures have failed, this method of Murray's can be employed with excellent results.

The same author recommends a similar procedure³ for acromioclavicular separations and uses two Kirschner transfixation wires in the acromion and outer third of the clavicle for immobilization. Phemister⁴ has modified this technic by advocating open reduction of the acromioclavicular joint and threaded wire fixation.

For fractures of the shaft of the humerus, Caldwell⁵ has proposed the hanging cast method of treatment, which in his hands has yielded very good results. A plaster cast is applied from the wrist to the base of the thumb with the elbow at right angles and the forearm in the position of midpronation. A wire loop is incorporated in the cast at the level of the wrist, and through this a bandage is passed that encircles the patient's neck. The hanging cast allows freedom of motion at the shoulder and is of sufficient weight in itself to afford any necessary traction. It is suitable for shaft fractures only; supracondylar and surgical neck fractures are not included in Caldwell's report. Since traction is the result of gravity in this method, it is important to warn the patient not to rest his cast on the arm of a chair or other support and to sleep at night with his body in the semiupright position.

As a general rule, the cast is retained for six weeks with gradually increasing motion as discomfort subsides. It is followed by a sling at 90° with light use of the arm and swinging exercises during the day. At the end of eight weeks all dressings can usually be removed, and at the end of

*Reprints of articles in this series are not available for distribution but the articles will be published in book form. The current volume is *Medical Progress Annual Vol. III 1942* (Springfield Ill no. 3 Charles C. Thomas Company 1942 \$5.00).

*Instructor in orthopedic surgery, Harvard Medical School, and orthopedic surgeon, Massachusetts General Hospital.

three months the patient should have full restoration of function.

A simple and effective method of treating fractures of the upper two thirds of the humerus has been reviewed by Gurd.⁶ The method is not new and has also been advocated by Eliason and others. It is included in this report because of its importance and need of re-emphasis.

Briefly, the treatment consists of placing a triangular pad under the axilla with a base which affords abduction of the arm of 15 degrees. The arm, shoulder and thorax are then incorporated in a plaster cast; the forearm is left free and is supported by a sling. The sling is removed in seven to ten days, and active motion of the elbow joint is begun. The cast is removed in two to five weeks; a cravat sling is supplied, and active use of the limb is advised. The method described has been used by the author for twenty years with satisfactory results, although no statistical study of end results has been made. It was not used for fractures of the anatomic neck or of the greater tuberosity of the humerus.

The treatment of fracture of the ulna associated with dislocation of the head of the radius (Monteggia fracture) has been greatly facilitated and improved by the work of Speed and Boyd,^{7, 8} who have described an excellent surgical approach to this problem and related their experiences in a series of 62 cases. The subject is ably presented and should be read in full by any surgeon especially interested in this fracture.

Fractures of the carpal scaphoid are often mistaken for a sprained wrist because of their failure to show a fracture line in the initial x-ray film. Thorndike and Garrey⁹ in a college clinic saw 17 cases, 11 of which had old or previously unrecognized fractures. The failure to demonstrate these fractures by roentgenograms, especially in the initial examination, has been frequently mentioned. They suggest that better views may be taken with the fist clenched and the fingers resting on the x-ray plate with the palm down in extreme ulnar deviation and extreme pronation. If a true undetected fracture is present and motion is permitted, absorption of the bone occurs along the fracture line, and the fracture becomes more evident in one or two weeks. Treatment of these fractures has become standardized and was recorded in the last progress report on fractures.¹⁰

A practical suggestion to improve the treatment of a badly comminuted Colles's fracture, in which it is difficult or impossible to maintain radial length by the usual position of ulnar deviation, is to employ skeletal traction on the thumb. A plaster cast is first applied to the broken wrist in the orthodox manner for immobilization of a reduced Colles's fracture, after which a heavy wire such as is used for coat hangers is shaped to extend

5 to 7 cm. beyond the tip of the thumb with its two free ends anchored in the plaster cast. This wire acts as a framework to which traction can later be applied. A fine Kirschner wire is then drilled through the proximal phalanx of the thumb and cut to sufficient length to engage in the loops of a light wire stirrup, which just covers the thumb end. Traction on this stirrup by means of rubber bands attached to the extended wire frame draws the thumb distalward, increasing the degree of ulnar deviation and pulling on the radial collateral ligament, which in turn draws the styloid process of the radius distalward into the desired position and holds it there until union takes place.

The results of treating fractures of the neck of the femur by means of internal fixation, as advocated originally by Smith-Petersen, are more gratifying as time goes on. The percentage of unions and of excellent function is increasing with experience and improved technic. From a comprehensive study¹¹ of the results of internal fixation of fractures of the neck of the femur by the Fracture Committee of the American Academy of Orthopedic Surgeons, it was learned that the Smith-Petersen nail was more efficient than nails of other types, pins or wires in respect to maintaining reduction, incidence of breaking, migration and percentage of bony union obtained.

It has been pointed out recently by Wilson¹² and Carrell¹³ that fractures of the neck of the femur in children are much more serious injuries than in adults, and the results on the whole have been very disappointing. This is probably due to the fact that adequate immobilization of the fracture cannot be obtained by plaster-cast fixation alone and that internal fixation cannot be employed in children because of the danger of injuring the epiphyseal line and arresting growth. An ideal method of treatment is so far unknown. Carrell thinks that, after reduction fixation is best secured by abduction, plaster and traction.

Interest has been centered recently on intertrochanteric fractures of the femur, chiefly because of their high mortality rate. Leydig and Brooks¹⁴ report a series of 302 cases at the St. Louis City Hospital in which the mortality rate was 39.3 per cent. Moreover, a survey of seven of the large private hospitals in St. Louis revealed a mortality of 25 per cent in 335 cases, over twice that implied in the literature and textbooks. Although this high mortality rate has not been experienced by all investigators, it is apparent that the rate for intertrochanteric fractures is much higher than that for femoral-neck fractures (11.6 per cent). In view of this fact, Leydig and Brooks attempted to treat a series of intertrochanteric fractures by fixation with a Smith-Petersen nail, but found that the im-

mobilization was inadequate and that in every case there resulted *coxa vara* and shortening of various degrees. For this reason, they employed a lag bolt instead of the nail, and report their present results as satisfactory.

For similar reasons, Thornton¹ has designed a combination Smith-Petersen nail and bone plate that secures the intertrochanteric fragments in an admirable way, preventing *coxa vara* and allowing early convalescence as in fractures of the femoral neck.

The status of the Roger Anderson method of treating fractures varies in different parts of the country. I have seen very few end results of this method and have no accurate statistics to go by. The only series of cases known to me was reported in an address by Dr. Charles Bradford, of Boston, who recently returned from the American Hospital in England, where there were 61 selected cases that were treated by the Roger Anderson method. Of these, 30 were in the femur, 16 in the lower leg, 3 in the humerus, 6 in the forearm, 5 in a metacarpal and 1 in the mandible. According to Dr. Bradford:

In the femur cases the alternative to using the Roger Anderson method was usually bone plating whereas in the tibia and fibula cases, the Roger Anderson method was considered to be excellent. For the humerus conservative treatment was considered advisable or bone plating, rather than the use of the Roger Anderson apparatus, and for forearm fractures the Roger Anderson apparatus was considered as being questionable in its value. For the mandible and metacarpal fractures, a miniature Roger Anderson apparatus had to be specially made.

Of the 61 cases treated, 43 were clean cases, 6 were potentially infected, and 12 were seriously infected. In the 43 clean cases treated by the Roger Anderson apparatus, there was no infection in the pin holes. The same can be said for the 6 potentially infected cases. Of the 12 seriously infected cases in 1 the pin tracks became grossly infected, in 7 the pin holes healed completely, and in 5 there were small draining sinuses.

As regards the end results of the 61 cases above mentioned, 3 had delayed union due to distraction of the bone fragments. Also it was noted that knee motion was limited frequently in fractures of the femur when the Roger Anderson appliance was employed, but not so much when used in the tibia and fibula fractures. After the application of the splint the patients were not supposed to put full weight upon their limbs but some did it anyway. In some cases, it was necessary to perform the reduction of the fracture in stages rather than all at one time.

Some of the drawbacks of the Roger Anderson method were the pin hole infections and of the one hundred and sixty pin holes concerned in these fractures a post-operative discharge was present in twenty. Also it was the feeling of the surgical staff that the method requires a special type of mechanically minded surgeon and unless the instrument is used properly it can give bad results. It is emphasized by those who have had experience with this treatment that the method is not an easy one and is really a hinder way to treat fractures

than by the usual standardized methods. Also when a comparative series of cases was treated at the Boston City Hospital at one time those treated by the Roger Anderson apparatus showed more delayed union than did those treated by the usual methods of skeletal traction or plaster casts.

Another serious disadvantage of the Roger Anderson method is that it requires a dangerous degree of exposure to x-rays, as has been demonstrated in clinics where the method is used.

On the other hand, when the Roger Anderson splint is applied properly in a successful case, the patient becomes ambulatory in a week or two so that, from the standpoint of evacuation of patients this method is an excellent one and especially applicable for war conditions.

The method of treating comminuted fractures of the patella by excision has spread into other fields of surgery, and one finds that complete removal of this bone is yielding favorable results in selected cases of arthritis, tuberculosis, chronic osteomyelitis, Pige's disease and traumatic osteochondritis.

An interesting and unusual fracture has recently been described by Hall.¹ It is located in one or more of the spinous processes of the lower cervical or upper dorsal vertebrae, and is called 'clay shoveler's fracture,' since it usually occurs in laborers while throwing up a shovelful of clay. The clay sticks to the shovel, the worker feels a sudden stab of pain and sometimes hears a crack between the shoulders, and is unable to continue working. The symptoms are pain between the shoulders, nearly always on one side of the midline and sometimes beneath one scapula. It is made worse on forward stretching of the arms or on attempting to pull or lift anything. Sometimes the pain goes up to the head or down the spine, and in a few cases it proceeds down the arm, which invariably feels weak. Also, the patient may hear a click on performing certain movements. Examination reveals tenderness of the spinous processes at the site of fracture and tenderness along the course of the rhomboid muscles. Likewise, mobility of the affected spinous process can usually be detected. Flexion of the head invariably produces pain. The diagnosis is mistaken in the majority of cases for muscle strain. In Hall's opinion, the treatment indicated is removal of the detached fragments.

TUBERCULOSIS OF BONES AND JOINTS

Two new methods of treatment of tuberculosis of the hip are worthy of mention. One is known as femoroischial transplantation and the other as 'femoroischial fusion.'

The former method is described by Bosworth¹ and is usually employed when the head and neck of the femur have been totally destroyed. An

oblique osteotomy is performed just above the level of the ischial tuberosity, and the sharpened end of the divided femoral shaft is inserted into the tuberosity of the ischium, which is split and levered apart for this purpose. When sinuses exist, the operation may be performed in two stages, the first stage being the removal of the diseased trochanter, neck and remnants of the femoral head plus granulation tissue and so forth, in an effort to obtain complete closure of all wounds.

The femoroischial fusion method has been described by Trumble¹⁸ and consists of ankylosing the lesser trochanter area of the femur to the tuberosity of the ischium by means of a bone graft. This is actually a form of extra-articular arthrodesis, and after union of the graft takes place, the disease in the hip joint proceeds to subside and eventually to disappear. The advantage of this type of fusion is that the operative site is sufficiently distant from the area of disease to allow good healing. The surgical approach is posterior, and is the same as the standard approach to the sciatic nerve under the gluteus maximus by reflecting the muscle from its insertion. A strong tibial graft is used to bridge the space between the ischium and femoral shaft.

In fusion of knee joints and ankle joints, Hatt¹⁹ recommends the use of a central bone graft, which he has found to be successful and not associated with any unfortunate complications or retardation of growth, even though the graft passes completely through both epiphyseal lines adjacent to the articular surfaces. This type of fusion is especially applicable to children, in whom the danger of arrested growth is always imminent. Hatt employs two special bayonet-shaped instruments to facilitate his operative procedure.

BONE TUMORS

Two new types of bone tumor have been described recently—namely, osteoid-osteoma and eosinophilic granuloma.

The former was reported by Jaffe²⁰ in 1935, and since that time he and Lichtenstein have collected 33 cases. They describe the lesion as being always small and affecting the substantia spongiosa or cortex of a single bone. It is often mistaken for sclerosing or nonsuppurative osteomyelitis. Roentgenogram interpretation of this tumor is discussed in detail in their paper,²¹ and the authors believe that the condition is a benign neoplasm.

The second new bone tumor, eosinophilic granuloma, has also been reported by Lichtenstein and Jaffe.²² It occurs in young persons, especially boys and young men, and mainly involves the calvarium, but it may occur in other bones, such as the ribs, femur, vertebrae, humerus and pelvis, the flat bones appearing to predominate. Green,

Farber and McDermott²³ have very recently presented 10 additional cases. Farber²⁴ suggests that the lesion is a variant of the basic process of which Hand-Schüller-Christian and Letterer-Siwe diseases are other examples, and disagrees with Lichtenstein and Jaffe in considering the condition a distinct new entity.

Roentgen examination of this tumor shows localized lesions starting in the medullary cavity and expanding and eroding the cortex. Single lesions simulate bone cysts, osteomyelitis or malignancy, while multiple lesions suggest multiple myeloma. Histologically, the tumors are characterized by phagocytosed eosinophils, with giant cells also present. There may be an eosinophilia of the blood, and a sternal biopsy may show many eosinophilic cells. So far as is known at the present time, the tumor appears to be benign, and the lesions have healed promptly after roentgen radiation, curettage or wide excision.

Revived interest in the treatment of osteogenic sarcoma has been aroused by Ferguson,²⁵ who made a detailed statistical study of 400 cases reported in the Registry of Bone Sarcoma of the American College of Surgeons. As a result of this study, he recommends the following treatment for osteogenic sarcoma: avoidance of early amputation ("early amputation is defined as amputation before the seventh calendar month after onset of symptoms"); irradiation before delayed amputation; irradiation, excision and implantation of a bone graft or bone chips before amputation, with amputation before the recurrence becomes evident; and repetition of excision, rather than amputation, if recurrence becomes evident before amputation can be done.

The author's conclusions are so contrary to our previously accepted conceptions of treatment that it is difficult to accept them at first hand. The facts that he presents, however, must be recognized and studied carefully with an open mind.

HIP CONDITIONS

Congenital Dislocation

Scaglietti²⁶ reports that at the Rizzoli Institute in Bologna, Italy, this condition was diagnosed during the first year of life in 736 cases and the patients treated by abduction. Excellent results were obtained in 93.9 per cent, which shows the great importance of early diagnosis. The value of diagnosing dislocation of the hip during the early months of life cannot be too strongly emphasized, and as an aid to this end, Burman and Clark²⁷ have described minutely the outlines and markings evident in roentgenograms of infants between twenty-six days and twelve months of age, certain of which aid in making the diagnosis.

In those cases in which a Schanz osteotomy is thought to be advisable, Unger and Waring²⁸ maintain that it is essential to hyperextend as well as to abduct the distal fragment of the femur in order to compensate for the lumbar lordosis, and they describe a method by which the amount of hyperextension can be measured.

Traumatic Dislocation

In traumatic dislocation of the hip, it has now been learned that, following reduction, aseptic necrosis of the femoral head results much more frequently than was supposed and should be counteracted if possible by avoidance of early weight bearing. Too early weight bearing should never be allowed in these cases.

In a recent paper on this subject, Banks²⁹ reports 9 cases and discusses the problem of early diagnosis of aseptic necrosis of the femoral head. When ever possible, he suggests that the extremity be protected from weight bearing by means of crutches for four to six months after the postreduction period of immobilization or recumbency. During this period, he thinks that repeated x-ray examinations will probably show whether the femoral head is dead or alive, and that, dependent on this fact, weight bearing should be permitted or prevented until final revascularization and replacement by new bone have been completed.

Calvé-Légg-Perthes Disease

It appears from the experimental work of Compere, Garrison and Fahey³⁰ that multiple drilling of the neck and head of the femur for the purpose of revascularization in cases of Calvé-Légg-Perthes disease is a questionable procedure because of surgical trauma to the capital and greater trochanteric epiphyses, which results in arrest of growth, deformity, shortening of the neck of the femur, irregular contour of the femoral head and coxa vara.

The more recent articles that have appeared on this disease show a definite tendency toward agreement regarding treatment and prognosis. The treatment which ensures the best results is rest in bed with elimination of any weight bearing. Nearly all authors now agree that the major deformities, consisting of flattening of the head of the femur, bowing of the neck and deformation of the acetabulum, are the direct results of weight bearing stresses during the course of the disease, and emphasize the necessity for continuous freedom from weight bearing from first suspicion of the disease until the process is completed. This usually requires from two to three years.

Slipped Upper Femoral Epiphysis

This condition, if discovered early before displacement takes place, can be treated successfully by nailing through a lateral incision. The results are practically perfect. Early recognition is the key to successful treatment. When the condition is seen in the more advanced stage, with displacement and the line of junction still distinctly visible, the surgeon should then choose between an open reduction of the displacement, with nail fixation, and an osteotomy. Great care is essential in the preservation of the blood supply of the head and neck of the femur. Manipulation under anesthesia is to be condemned. In the late stages of this condition, osteotomy is considered by many to be the preferred procedure, but if not successful it should be followed by a cup arthroplasty.

Osteoarthritis

In the treatment of this common ailment, a variety of methods have previously been considered, such as manipulation, drilling, cheilectomy, osteotomy, acetabuloplasty, reconstruction procedures and arthrodesis. To this formidable list, another procedure offered by Smith Petersen³¹ can now be added, which will probably prove to be the most successful of all, namely, vitallium cup arthroplasty. This operation is standing the test of time and offers more hope of relief than any of the other procedures. It seems likely that vitallium cup arthroplasty and arthrodesis should be the two main procedures to choose between in the treatment of this condition, and that the decision should be made according to the individual patient's age, occupation and characteristics.

MISSCELLANEOUS CONDITIONS

Torticollis

It appears from recent reports in the literature³² that division of both ends of the sternocleidomastoid muscle is a more efficient treatment for torticollis than severing only one end, and also does away with the necessity of postoperative retention apparatus, such as plaster casts or splints.

Intervertebral Disk

One of the serious objections to the use of iodized oil in myelography has been its possible irritating effects, and for this reason there has been a tendency to employ the less reliable procedure of pneumomyelography when making the diagnosis of ruptured intervertebral disk. Recently however, Kubik and Hampton³³ reported a simple method for the removal of the iodized oil from the subarachnoid space thus doing away with

any possible danger from its continued presence there. The oil is introduced by lumbar puncture with the patient on the fluoroscopic table, leaving the needle in place during the examination, and removing the oil immediately afterward. This improvement in diagnostic procedure represents a great advance in the attack on the problem of intervertebral-disk injuries.

The end results of treatment in 139 patients with protruded disks in the lumbar spine have been carefully analyzed by Barr and Mixter³⁴ who state that 77 per cent of the patients had complete relief from their radiating pain, and an additional 18 per cent had only minor discomfort in the affected leg; in other words, the relief from the sciatic pain was satisfactory in 95 per cent of the cases. About one third of the patients had their spines fused at the time of laminectomy, the other two thirds having laminectomy alone with removal of the protruding disk fragment. It is interesting and important to note that 73 per cent of the patients having fusion considered their backs of normal strength, whereas only 52 per cent of those without fusion had no complaints. Where insurance compensation was involved, it was found that after operation 45 per cent of the compensation patients went back to their original occupation and considered themselves fully recovered, 30 per cent went back to lighter jobs, and 25 per cent continued to receive compensation or had litigation pending. The fact that 75 per cent of these patients returned to some type of work is encouraging, and should justify co-operation from insurance companies in the attempt to rehabilitate otherwise totally incapacitated patients.

Scoliosis

Some very interesting and discouraging facts concerning idiopathic scoliosis have been brought to light by the Research Committee of the American Orthopaedic Association,³⁵ which reviewed 425 cases in sixteen orthopedic clinics from an end-result standpoint. The committee found that the disease appeared most frequently at the time of puberty, and predominated in girls in a ratio of 4:1. Curvature was to the right in 80 per cent of the patients. All types of treatment were encountered, but complete correction of the spinal curve was gained in only 5 per cent of the corrected cases, all the correction was maintained in 8 per cent, and there was complete loss of correction in 29 per cent. The incidence of pseudoarthrosis for the entire operative group amounted to 28 per cent. The conclusions drawn from this very careful and illuminating study were as follows: practically none of the patients with scoliosis were cured, if correction of lateral deviation is a criterion; in approximately 60 per cent of those

treated by exercises the deformity increased, and in 40 per cent it remained unchanged; in the majority of cases correction without fusion resulted in complete loss of correction after support was discontinued; and correction by the turnbuckle jacket and subsequent fusion yielded better results than did other types of treatment.

Volkmann's Ischemic Contracture

The general impression is gaining that Volkmann's ischemic contracture should be considered to have a vasomotor origin. Numerous authors have emphasized this feature of the condition and have reported obliteration of the lumen of the brachial artery at the time of operative exploration. The removal of the tunica adventitia with its sympathetic fibers from the artery has resulted in the return of circulation in nearly all cases. Luzuy³⁶ reports two cases, and believes that in the absence of neural lesions the condition should be treated by injecting procaine hydrochloride into the stellate ganglion. Griffiths³⁷ thinks that the syndrome is due to injury of arteries and to accompanying spasm of the collateral circulation. He suggests the intravenous use of papaverine and adds that, if this fails, the contused or lacerated portion of the artery should be excised between ligatures. From the above and other recent reports, it would seem logical that a sympathetic block by novocain might be effective in removing the arterial spasm in many cases, and overcome the condition without resorting to radical surgery. This tendency to consider Volkmann's contracture an arterial spasm is undoubtedly a step in the right direction and advances knowledge regarding this very serious and crippling disorder.

Sulfonamides

The advent of the sulfonamides in the field of surgery has opened up possibilities beyond our imagination. Already we are taking advantage of their aid in overcoming wound infections and septicemia. War wounds have demonstrated their beneficial effects in a striking way, and surgical literature is full of data concerning the use of these drugs. It is not the function of this paper to discuss the relative merits of the different sulfonamide drugs in the treatment of compound fractures, osteomyelitis and war wounds, but only to state that, to date, it would appear that sulfanilamide is the substance of choice to introduce into open wounds as a bacteriostatic agent. In addition to this, one must always keep in mind the supreme importance of careful débridement and mechanical cleansing, the use of saline instead of iodine or alcohol as a cleansing solution, the value of plaster-of-Paris immobilization and the advantages of infrequent dressings.

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Stated Meeting, October 7, 1942

A STATED meeting of the Council of the Massachusetts Medical Society was called to order at 10:30 a m in John Ware Hall, 8 Fenway, Boston, on Wednesday, October 7, 1942, by the president, Dr. George Leonard Schadt, Hampden, 196 councilors were present (Appendix No. 1).

The records of the annual meeting held on May 25 and 26, 1942, as published in the June 25, 1942, issue of the *New England Journal of Medicine*, were presented by the Secretary.

The vice president, Dr. Peirce H. Leavitt, moved their acceptance. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

REPORT OF EXECUTIVE COMMITTEE

This report (Appendix No. 2) was presented by the Secretary. He announced that the committee held two meetings during the summer, one a special session, held on July 10, and the other a regular meeting, held on August 26.

The meeting of July 10 was called by the president, Dr. George Leonard Schadt, in consequence

of a letter received from Dr. Frank H. Lahey, chairman of the Directing Board of the Procurement and Assignment Service. This letter was by way of an answer to a resolution offered by Dr. Reginald Fitz, state chairman of the Procurement and Assignment Service, and adopted by the Massachusetts Medical Society at its annual meeting on May 26, 1942. The Society, by this resolution, memorialized the Surgeon General, the Directing Board of the Procurement and Assignment Service and others for the purpose of making available for commissions in the medical corps of the armed forces a certain pool of physicians in Massachusetts who had been declared ineligible for such commissions. The committee recognized that the acceptance of the proposition submitted in Dr. Lahey's letter would involve the amending of the by-laws of the Massachusetts Medical Society. The committee further took notice of the fact that such an amendment could not be effective until passed on by the Society in May, 1943, a date much too late to be of use as a means of meeting what was then represented as an emergency.

The Secretary then spoke of the correspondence that followed with the Procurement and Assignment Service and the Office of the Surgeon General, which culminated in an agreement between the Massachusetts Medical Society and the office of the Surgeon General whereby the Surgeon General would include in the papers to be executed by the graduates of unapproved medical schools who applied for commissions in the Army the following form:

	Place	
	Date	
Dr.	of	
is known to this society as a graduate of		
Medical School, located in		He is
engaged in the practice of medicine in Massachusetts,		having been licensed by this state since
He is, so far as is known, an ethical practitioner of medicine. He would be eligible to apply for membership in the Massachusetts Medical Society if he had been in practice for five years. Having attained such membership, he would be accredited to the		District
Medical Society.		
Signed		, Secretary
		District Medical Society

N.B. The applicant should bring his diploma and certificate of licensure to the district secretary.

The Secretary said that the Executive Committee had approved of this arrangement and moved that the Council do likewise. This motion was seconded by Dr. Charles J. Kickham, Norfolk, and it was so ordered by vote of the Council.

The Executive Committee, acting on the recommendation of the Committee on Membership, restored four former fellows to membership, denied the petition of one fellow to be so restored and allowed one fellow to change his membership from one district to another without changing his place of residence.

The report spoke in the highest terms of a report on state-aided cancer clinics by Dr. Channing C. Simmons, of Newton. The Council extended a rising vote of thanks to Dr. Simmons for his work in connection with this report.

The committee spoke of having reviewed the report of the Committee on Cancer, submitted by the chairman, Dr. Shields Warren, Suffolk. The committee approved the recommendations contained in this report.

The committee reviewed the report of the Committee on Public Relations, submitted by the secretary, Dr. Elmer S. Bagnall, Essex North. The committee approved the recommendation contained in this report.

The committee voted to lay on the table a letter from Mrs. John L. Bauer. This letter had been referred to the committee by the Council and

had to do with the formation in Massachusetts of a ladies' auxiliary to the American Medical Association.

Action on the petition of Dr. Frank R. Ober, Suffolk, past president, that two delegates be appointed to the annual meeting of the Associated State Postgraduate Committees was postponed.

The committee on the petition of Dr. Dwight O'Hara, Middlesex South, recommended the discontinuance of the Committee Appointed to Study the Practice of Medicine. The Secretary moved the adoption of this recommendation. The motion was seconded by a councilor, and it was so ordered by vote of the Council.

The committee, on the recommendation of Dr. Henry R. Viets, of Boston, recommended the discontinuance of the Committee on Army Medical Library and Museum. The Secretary moved the adoption of this recommendation; the motion was seconded, and it was so ordered by vote of the Council.

The committee voted to lay on the table the petition of Dr. Leroy E. Parkins, Suffolk, that the Council of the Massachusetts Medical Society request the American Medical Association to change the place of its annual meeting from San Francisco to some city in the Middle West.

The committee endorsed the work of the National Physicians Committee for the Extension of Medical Care and recommended that the Council of the Massachusetts Medical Society do likewise. The Secretary moved the adoption of this recommendation; the motion was seconded, and it was so ordered by vote of the Council.

The committee considered a plan offered by the Yankee Network intended to inform the public of the necessity of conserving doctors' time and energies during these times. The committee voted not to accept this plan.

The report spoke of a proposal of Dr. W. Richard Ohler, of Jamaica Plain, and others that the Massachusetts Medical Society enter in joint sponsorship with Harvard, Tufts and Boston University medical schools whereby postgraduate instruction might be provided for the medical officers of the Army and Navy on active duty within the confines of Massachusetts. The committee approves this proposal and recommends its adoption. The Secretary moved the adoption of the recommendations; the motion was seconded, and it was so ordered by vote of the Council.

The committee approved of certain ad-interim appointments made by the President.

The Secretary moved the adoption of the report as a whole. The motion was seconded by a councilor, and it was so ordered by vote of the Council.

REPORTS OF STANDING COMMITTEES

Arrangements (Dr. Gordon M. Morrison, Middlesex South, chairman)

This report (Appendix No. 3) was presented by Dr. Morrison.

He announced that the annual meeting will be held on May 17, 18 and 19, 1943, at the Hotel Kimball in Springfield. The annual meeting of the Council will be held on the evening of May 17.

Dr. Ralph R. Stratton, Middlesex East, moved the acceptance of the report. The motion was seconded by a councilor, and it was so ordered by vote of the Council.

Publications (Dr. Richard M. Smith, Suffolk, chairman)

No report.

Membership (Dr. Harlan F. Newton, Suffolk, chairman)

No report.

Finance (Dr. John Homans, Suffolk, chairman)

Dr. Homans said his committee was offering no formal report. He pointed out that, under the new by laws, chairmen of committees that will need funds to prosecute their work must prepare budgets that they must send to the Committee on Finance. The budget so presented must specify the purpose of all expenditures of \$100 or more.

He said that he had already sent out to the chairmen of the various committees a preliminary form, which would be of aid to them in reporting their proposed expenditures.

He pointed out that there was no provision in the by laws which made it mandatory for the officers of the Society to submit a budget. He added, however, that it was his opinion that there would not be much difficulty in this direction.

Dr. Carl Bearse, Norfolk, moved the adoption of this report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Ethics and Discipline (Dr. Ralph R. Stratton, Middlesex East, chairman)

No report.

Medical Education (Dr. Robert T. Monroe, Norfolk, chairman)

This report (Appendix No. 4) was offered as a preliminary report. A final report on the nursing situation produced by the War will be offered at the next meeting of the Council.

Dr. Monroe pointed out that the armed forces have asked for 60,000 registered, single nurses, forty five years or younger, who are in good physi-

cal condition. The committee believes that this demand can be met, pointing out, however, that this will create a shortage of nurses for civilian needs. The necessity of lowering the educational and training standards for graduate nurses, nevertheless, is not at hand. Future needs may possibly make such changes necessary.

The report mentioned the excellent work done by the Red Cross nurses' aides. A wider utilization of the attendant nurse was urged, and it was recommended that a campaign be begun at once to train large numbers of such nurses. The committee does not believe that such training should go on side by side with the training of the graduate nurse. The report further stated, however, that such an experiment is being tried at the Beverly Hospital.

Dr. Albert A. Hornor, Suffolk, moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Public Health (Dr. Francis P. Denny, Norfolk, chairman)

No report.

Medical Defense (Dr. Arthur W. Allen, Suffolk, chairman)

No report.

Society Headquarters (Dr. William H. Robey, Suffolk, chairman)

No report.

Industrial Health (Dr. Dwight O'Hara, Middlesex South, chairman)

This report was as follows:

Each of the committee's meetings has been attended by a representative of the State Department of Public Health and by the director of the Division of Occupational Hygiene of the State Department of Labor and Industries. Other meetings have also been honored by the presence of a member of the Council of Industrial Health of the American Medical Association, the president and secretary of the Massachusetts Medical Society and the state chairman of the Procurement and Assignment Service. The committee has also had the hearty co-operation of the editor of the *New England Journal of Medicine* and has made contact with the Associated Industries of Massachusetts.

With these reinforcements the committee has been able to visualize some of the problems now faced and about to be faced in industrial health in this state. An attempt has been and is being made to express these problems to the fellows of the Society by the publication of announcements and editorial comments in the pages of the *New England Journal of Medicine*. One of these editorials has been reprinted in full in *Industrial Medicine*, one of the nation wide manufacturers' publications.

This reinforcement of the committee also enabled it to secure, distribute and publicize to every doctor in Massachusetts a copy of the pamphlet, *Manual on Industrial Health for Defense*, prepared by the Massachusetts Committee on Public Safety.

On August 17 the committee voted that it "constitute itself as an agency to gather what information it can concerning doctors who may be available for industrial work and also information concerning possible placements for such doctors, working of course in co-operation with the Procurement and Assignment Service and with due regard for other than industrial need for medical service." Subsequently those doctors who indicated on their Procurement and Assignment blanks a primary interest in industrial practice have been invited to register with the committee. Of about 600 doctors, 260 had responded on October 4. The information thus obtained is being transferred to a punch-card system and will be available in case inquiries appear from industrial plants looking for medical service. To date there has been only one such inquiry, and it is likely that there is not as yet an acute shortage of industrial medical service. If such a shortage develops, however, or if the needs of industry rapidly expand in Massachusetts, the committee hopes to be in a position to be helpful.

The committee has also voted to hold a full-day "institute" on industrial health this fall and, with the help and co-operation of the Committee on Postgraduate Education, is preparing a program for Saturday, November 7, morning, afternoon and evening, at the Harvard Club of Boston. The committee is very much aware that no single program can cover the urgent matter in the field and is therefore hoping that the need and the interest may be sufficiently localized profitably to repeat or amplify this type of activity. Much more ambitious programs are under way in other parts of the Nation, and it may be that this method will prove itself a valuable one in the near future. At the moment, the committee is most perplexed to know how to reach the particular physicians who are most vitally concerned and strategically placed to make the largest contributions—those who are employed on part time or only casually in the small plants that are now rushing war production. Such plants employ three quarters of the labor in this state, but utilize an ever so much smaller fraction of the medical supervision that might be made available to them.

It was moved by Dr. Homans and seconded by a councilor that the report be accepted, and it was so ordered by vote of the Council.

REPORTS OF SPECIAL COMMITTEES

Public Relations (Dr. Elmer S. Bagnall, Essex North, secretary)

This report (Appendix No. 5) spoke of a conference which the committee had had with Mrs. Emma Tousant, chairman of the Industrial Accident Board. Out of that conference came the following recommendation by the committee:

Your committee recommends that the President be authorized to appoint a subcommittee (not necessarily limited to the membership of the Committee on Public

Relations) to confer with the newly appointed Medical Advisory Committee of the Industrial Accident Board to see what should be done and can be done to improve certain aspects of the medical administration of the Act, particularly those related to hospitalized cases.

Dr. Bagnall moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Dr. Carl Bearse moved the adoption of the recommendation contained in the report of the Committee on Public Relations. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Tax-Supported Medical Care (Dr. Bagnall, chairman)

This report was as follows:

The Committee on Tax-Supported Medical Care has had no meetings since the last meeting of the Council. Matters are being referred by the Department of Public Welfare at the State House for consultation. These are being handled in some instances by reference to a special committee in the district concerned and decisions concerning policy are being satisfactorily arrived at.

This is the course the committee plans to follow pending developments that would indicate more active operations.

Dr. Bagnall moved the adoption of this report. The motion was seconded by a councilor, and it was so ordered by vote of the Council.

Postpayment Medical-Care Costs through Banks (Dr. Bagnall, chairman)

Dr. Bagnall stated that, since the last meeting of the Council, the Bankers Association has had a committee working on the further shaping of the plan for installment payments; when they are ready for action the committee will proceed jointly with them to commence operations.

Dr. Bagnall moved the adoption of this report. The motion was seconded by a councilor, and it was so ordered by vote of the Council.

Prepayment Medical-Care Costs Insurance (Dr. James C. McCann, Worcester, chairman)

Dr. McCann presented the report (Appendix No. 6). It was moved and seconded that the report be accepted, and it was so ordered by vote of the Council.

Procurement and Assignment (Dr. Reginald Fitz, Suffolk, chairman)

Dr. Fitz announced (Appendix No. 7) that one of the members of his committee, Dr. John J. Curley, Worcester North, had entered the Army, having been commissioned a major in the Medical Corps. He spoke of how valuable had been Ma-

for Curley's contribution to the work of this committee. He added that Dr Bartholomew P Sweeney, Worcester North, had taken Major Curley's place on the committee.

He spoke of the distribution of physicians in Massachusetts, as of the year 1941, and offered a table to supplement his remarks.

He said that the figures in the table suggested that the majority of members of the Society had filled out their enrollment forms. He added, however, that only 70 per cent of the 7713 doctors in the State had done so. He emphasized the need of the Army and Navy for young medical officers. He said that a random selection of 100 enrollment forms of physicians thirty-five years of age or younger showed that one third of them hoped to continue in private practice. Most of the latter group, however, were married and had dependents.

He expressed the thought that at this time there was no real medical depletion in the State. He said that this matter is being carefully watched and that machinery is at hand to prevent it or to cure it, if it arises.

He added that the medical problem of industry is beginning to assume a larger significance than heretofore. He added that his committee would soon be in a position to help industry find needed qualified doctors.

He said that the much debated question of the fate of graduates of substandard schools, licensed to practice medicine in Massachusetts, had been solved.

He believed that the work of the committee was progressing slowly but steadily along well-ordered lines. He spoke in a commendatory manner of the co-operation that the committee was receiving from the district committees, hospitals, medical schools and public health officials.

Dr Fitz moved the acceptance of the report. The motion was seconded, and it was so ordered by vote of the Council.

Survey of State Aided Cancer Clinics (Dr Channing C Simmons, of Newton)

The President announced that, inasmuch as each councilor had received in advance copy of this report (*New England Journal of Medicine*, issue of September 17, 1942, page 458), it was offered only by title.

Dr Shields Warren, Suffolk, moved its adoption. This motion was seconded, and it was so ordered by vote of the Council.

It was moved by Dr Hilbert F Day, Middlesex South, that a rising vote of thanks be extended to Dr Simmons in appreciation of his work. This motion was seconded by Dr Phippen, and on a standing vote, it was so ordered by the Council.

Cancer (Dr Shields Warren, Suffolk, chairman)

This report (*New England Journal of Medicine*, issue of September 17, 1942, page 462) made the following recommendations:

That the Council thank Dr Simmons for his services.

That it is advisable to suggest to the Department of Public Health the maintenance of existing clinics with the following exceptions: the state aided clinics at Quincy and at Newburyport should be discontinued.

That particular study be made of the clinics in Brockton, Greenfield, Pittsfield, Springfield and Hyanus to determine whether they can be more active and of greater service to their communities. (The physicians in these communities are now being interviewed to obtain their opinions of the clinics and their suggestions.)

Dr Warren moved the adoption of the recommendations. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Postgraduate Instruction (Dr Reginald Fitz, Suffolk, chairman)

The committee's report was as follows:

The committee voted unanimously to discontinue the usual extension courses and the New England Postgraduate Assembly during the current year.

The committee has assisted the Committee on Industrial Health in developing a postgraduate institute on industrial problems in medical practice, which will be given at the Harvard Club of Boston on Saturday, November 7. The program will be published in the *New England Journal of Medicine* next week, also it will be mailed to every physician in Massachusetts.

The committee will continue to study current needs for postgraduate instruction and will report progress at the next meeting of the Council.

Dr Fitz moved the acceptance of this report. The motion was seconded by a councilor, and it was so ordered by vote of the Council.

Physical Therapy (Dr Franklin P Lowry, Middlesex South, chairman)

No report.

Expert Testimony (Dr Frank R Ober, Suffolk, chairman)

Dr Ober offered a verbal preliminary report, in which he said:

We have had one meeting of the committee, at which all members were present, and it was voted that we obtain all possible information from the state societies in the country and the American Medical Association. I received a large package of material from the American Medical Association a few days ago, and I was told that it would have to be returned in six days. It is obviously impossible for the committee to absorb all the material in six days, and so I am having reprints sent from different organizations from which these publications came, and we hope to have a regular report for the February meeting of the Council.

Dr. Ober moved the adoption of the report. The motion was seconded by a councilor, and it was so ordered by vote of the Council.

Automobile Insurance Claims (Dr. Henry C. Marble, of Boston, chairman)

No report.

Convalescent Care (Dr. T. Duckett Jones, of Brookline, chairman)

No report.

Committee to Study the Practice of Medicine by Unregistered Persons (Dr. Richard Dutton, Middlesex East, chairman)

No report.

Committee to Meet with Massachusetts Hospital Association (Dr. Walter G. Phippen, Essex South, chairman)

Dr. Phippen reported as follows:

The committee appointed to confer with a committee from the Massachusetts Hospital Association had referred to it the following vote of the Council:

We believe that insurance cases (Blue Cross, Workmen's Compensation, automobile accidents and prepayment medical-costs insurance) should be submitted to hospitals in the care of their physician of choice. About half the hospitals of this state now provide this "private ward" privilege. The practice is almost universal outside the Atlantic Coast states. We recommend that the Council instruct the Committee to meet with the Massachusetts Hospital Association to see whether there can be agreement on a state-wide policy in this matter.

Dr. Charles Wilinsky, the president of the Massachusetts Hospital Association, was notified, and on August 12 a joint meeting of the two committees was held. There was free and open discussion by all members present. It was believed that there might rightly be considerable difference of opinion among hospitals and among the medical profession at large concerning the advisability of treating private patients in free wards of hospitals. It was thought, however, that since this type of service was apparently desired by members of the low-income group and since it could be paid for by various types of insurance it probably must be accepted. The hospital group stated very strongly, however, that in selling the Massachusetts Medical Service ward plan it must be made very clear that, unless the recipients are protected by a Blue Cross policy, they must assume the regular ward cost as determined by each individual hospital. It was also emphasized that the presence of a considerable number of private patients of many doctors in the wards of hospitals accredited for training of interns might materially interfere with this educational program.

Therefore, the following recommendations were adopted:

(1) Whenever possible, insurance cases (Workmen's Compensation, industrial accident, automobile accident, Blue Cross and Blue Shield) be segregated in special wards.

(2) Members of the Massachusetts Medical Service (Blue Shield) ward plan should be informed that they will be accepted to pay the prevailing ward rate to the hospital unless they have Blue Cross ward-plan insurance.

(3) Nothing in the operation of the Blue Shield plan shall interfere in any way with the standards of professional care established by the staffs and trustees of the various hospitals. This shall also include the standards set for the training of interns. Nor shall rules laid down by the hospitals for the admission of patients be altered under this plan.

(4) Nothing in the plans of prepaid insurance for medical care shall conflict with the existing policies of the various hospitals.

(5) The two committees strongly recommend that the hospitals throughout the Commonwealth co-operate with the Blue Shield, so far as possible.

Dr. Phippen moved the acceptance of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Dr. Phippen moved the adoption of the recommendations contained in this report. The motion was seconded by Dr. Richardson, and it was so ordered by vote of the Council.

Committee to Examine WPA Records (Dr. Guy L. Richardson, Essex North, chairman)

Dr. Richardson offered the following report and moved its adoption:

A change in the method of handling the work of the committee has seemed advisable. The members of the committee were making regular visits to the WPA office to confer with Mr. Burns—state compensation officer. Because of the marked and continued decrease in the number of WPA employees and the consequent reduction in accident cases, together with the many added duties of all of us as physicians, a letter was sent to Mr. Burns advising him that we should not confer regularly at his office but should keep the contact by correspondence, and be available for conference when any matter came up which could not be settled properly by letter or telephone.

To quote from Mr. Burns's reply to our letter, which he dated September 2, the last two paragraphs may be of interest:

Strictly speaking, the Division has been markedly free of any controversial matter, and the volume of work has decreased to practically nothing. In making up this month's report I find that only 203 cases were registered for the month of August. I well recall the time when this would represent a single day's receipt.

Of course, we have less than 18,000 employed all over the State, which is only about 13 per cent of our former personnel. Indeed, if I have any problem, I shall seek your assistance without delay. Thank you for all the splendid co-operation given our organization by the Massachusetts Medical Society.

The motion was seconded, and it was so ordered by vote of the Council.

Maternal Welfare (Dr Judson A. Smith, of Newton, chairman)

No report

Rehabilitation (Dr William E. Browne, Suffolk, chairman)

Dr Browne reported (Appendix No 8) that his committee had in every way co-operated with the Massachusetts Selective Service Headquarters. He said that it seemed improbable that the federal government will, in the near future, undertake any extensive program of rehabilitation. When and if the Government does enter into such a program, the Massachusetts Medical Society, through this committee, will be ready to co-operate in an efficient manner.

Dr Browne moved the acceptance of the report. The motion was seconded by a counselor, and it was so ordered by vote of the Council.

Committee to Aid the Boston Medical Library (Dr William H. Robey, Suffolk, chairman)

Dr Robey said the committee had nothing definite to report.

APPOINTMENTS

The president offered the following appointments:

AUDITING COMMITTEE

Dr Francis C. Hall, of Brookline, chairman
Dr Burton E. Hamilton, of Brookline

COUNCIL

Dr George L. Gabler, Hampden, replacing Dr Stanley C. Cox, deceased
Dr G. Colket Caner, Suffolk, replacing Dr Roger I. Lee, who has become a member *ex officio*
Dr Merrill C. Sosman, Suffolk, replacing Dr Marshall N. Fulton, resigned
Dr John F. Casey and Dr Madeline R. Brown, Middlesex South, replacing Dr Dwight O'Hara and Dr Eliot Hubbard, Jr, who have become members *ex officio*
Dr Sumner H. Remick, Middlesex South, replacing Dr Roy D. Halloran, resigned
Dr George A. Buckley, Plymouth, replacing Dr Peirce H. Leavitt, who has become a member *ex officio*
Dr Herman D. Bone, Worcester North, replacing Dr John J. Curley, resigned
Dr Herbert Coulson, Essex North, replacing Dr David W. Wallwork, resigned

BOARDS OF CENSORS

Dr Andrew J. Leddy and Dr William M. Stobbs, Bristol North, replacing Dr William H. Bennett and Dr Curtus B. Kingsbury, resigned
Dr William W. Ferrin, Essex North, replacing Dr Arnold P. George, resigned

COMMITTEE ON EXPERT TESTIMONY

Dr Frank R. Ober, chairman, replacing Dr George Leonard Schadt, resigned
Dr William J. Brinkley, replacing Dr James J. Goodwin, resigned

COMMITTEE ON ARRANGEMENTS

Dr Gordon M. Morrison, chairman (already a member)
Dr Sidney C. Wiggan, Dr Robert H. Barker and Dr Richard I. Smith, replacing Dr James A. Halsted (chairman), Dr George P. Sturgis and Dr Henry H. Faxon, resigned

COMMITTEE ON REHABILITATION

Dr John Fallon, replacing Dr David C. Dow, deceased

VOTING MEMBERS IN MASSACHUSETTS HOSPITAL SERVICE, INC.

Dr Donald Munro, replacing Dr Richard P. Stetson, resigned
Dr Ralph R. Stratton, replacing Dr James A. Halsted, resigned

COMMITTEE ON MEDICAL DEFENSE

Dr Ira M. Dixon, replacing Dr George S. Reynolds, resigned

COMMITTEE TO MEET WITH MASSACHUSETTS HOSPITAL ASSOCIATION

Dr Edward A. Adams, replacing Dr Reynolds, resigned

COMMITTEE TO AID THE BOSTON MEDICAL LIBRARY

Dr William H. Robey, chairman
Dr Charles S. Butler
Dr David Cheever
Dr Michael A. Tighe
Dr Shields Warren

COMMITTEE TO MEET WITH THE ADVISORY COMMITTEE OF PHYSICIANS APPOINTED BY THE INDUSTRIAL ACCIDENT BOARD

Dr Daniel J. Ellison, chairman
Dr Gordon M. Morrison
Dr David D. Scannell

COMMITTEE TO WORK OUT THE NECESSARY ARRANGEMENTS FOR POSTGRADUATE WORK FOR THE ARMY AND NAVY

Dr W. Richard Ohler, chairman
Dr Chester S. Keefer
Dr Samuel H. Proger
Dr Leroy E. Parkins
Dr Frank R. Ober

Dr Albert A. Hornor, Suffolk, moved confirmation of these appointments. This motion was seconded by Dr Homans, and it was so ordered by vote of the Council.

MISCELLANEOUS BUSINESS

The President announced that two members of the Council had died since the last meeting.

Dr. Stanley C. Cox, of Holyoke, died June 7, 1942, in his sixtieth year.

Born in South Hadley Falls, he received his degree from University of Michigan Medical School in 1910. For twenty-one years, he served as associate medical examiner and medical examiner for the third district of Hampden County. He was head of the local medical division of the Massachusetts Committee on Public Safety in Holyoke. He was a member of the American College of Surgeons, and a fellow of the American Medical Association.

Dr. Cox is survived by his widow, two sons and three daughters.

Dr. David C. Dow, of Cambridge, died May 27, 1942, in his sixty-eighth year.

Born in Cambridge, he received his degree from Tufts College Medical School in 1898. He was an intern at the Cambridge Hospital, where he was a member of the staff until his retirement a year ago. He was medical examiner of the First District of Middlesex County, and was a member of the American Medical Association.

Dr. Dow is survived by his widow, a son and a daughter.

At the request of the President, the Council stood in silence for one minute in tribute to the memory of Dr. Cox and Dr. Dow.

Dr. Bagnall, as a preliminary to offering a motion, said that he was a little bit concerned about the organization of the medical profession and the instruction of the public to meet the approaching shortage of doctors. He said that in Haverhill all men under forty-five years, except one, have volunteered for service. He added that this naturally placed a very much greater burden on the older men. He said that if the standards of medical care were to be maintained, it was necessary that the public be educated to conserve doctors' energies.

Dr. Bagnall then moved that the President be authorized to appoint a committee, the number of the committee to be at his discretion, to look into this subject for report to the Council at a later meeting. This motion was seconded by Dr. Fitz, and it was so ordered by vote of the Council.

Dr. James C. McCann, Worcester, was at this point recognized by the chair. He asked the councilors present to do what they could to stimulate their associates to sign the contract submitted by the Blue Shield. He added that these signed contracts were coming in at the rate of about one hundred each day; in all, about one thousand had been received.

Dr. Hornor asked the following question: "Why should an internist sign this contract?"

Dr. McCann replied as follows:

That, of course, is always an important point because internists will not come fully into the program until we have a more complete contract available for the

public. But the reasons for signing are two. For the most part, this contract goes down through the specialties. It does overlap into x-ray; it overlaps into the general man's work who is doing any orthopedics or obstetrics or any anesthesia. Those are the principal things covered. It also overlaps, but to a very minor degree, in the field of the man who is doing a medical consultation practice. Now, those are reasons forming one basis for considering participation. The other basis is that, since the Society at large has undertaken this thing as the Massachusetts Medical Society's corporation and has presented it to the public from that angle, the mere endorsement of it by a large segment of the profession, including the internists, will mean a great deal toward success. The Society has about 5700 members, and if a large proportion were to sign their contracts it would strengthen the initial step and lead to inevitable success, and we should be able to say to the public that we had a broad participation in it by the physicians of the State. Those are the only reasons I know.

At this point in the meeting, Dr. Peirce H. Leavitt, vice-president, assumed the chair and Dr. Schadt addressed the Council for the purpose of backing up everything Dr. McCann had said in answering Dr. Hornor's question. Dr. Schadt urged everybody to sign up so as to give emphasis to the fact that the Blue Shield is backed by the Massachusetts Medical Society.

Dr. Schadt returned to the chair.

Dr. Leavitt moved that local committees on membership be advised and urged to investigate carefully and examine all candidates in regard to their ethics and methods of practice. This motion was seconded by Dr. Walter H. Pulsifer, Plymouth, and it was so ordered by vote of the Council.

At 12:30 p.m., Dr. Carl Bearse, Norfolk, moved that the meeting adjourn. This motion was seconded by Dr. Harry F. Byrnes, Hampden, and it was so ordered by vote of the Council.

MICHAEL A. TIGHE, *Secretary*

APPENDIX NO. 1

ATTENDANCE

BARNSTABLE	H. E. Perry
J. G. Kelley	C. C. Tripp
W. D. Kinney	
BERKSHIRE	ESSEX NORTH
J. J. Boland	E. S. Bagnall
Solomon Schwager	L. R. Chaput
	Herbert Coulson
BRISTOL NORTH	E. H. Ganley
W. H. Allen	H. R. Kurth
J. H. Brewster	P. J. Look
R. M. Chambers	R. C. Norris
	G. L. Richardson
BRISTOL SOUTH	F. W. Snow
G. W. Blood	C. F. Warren
R. B. Butler	
E. D. Gardner	ESSEX SOUTH
F. M. Howes	Bernard Appel
	H. A. Boyle

C P Brown
D S Clark
Loring Grimes
P P Johnson
B B Mansfield
A E Parkhurst
O S Pettingill
W G Phippen
H G Pope
E D Reynolds
J W Trask
C F Twomey
C A Worthen

FRANKLIN

A W Hayes
W J Pelleuter
H G Stetson

HAMPTON

E P Bagg
H F Byrnes
J L Chereskin
A J Douglas
E C Dubois
Adolph Franz, Jr
P E Gear
Frederic Hagler
G D Henderson
Charles Jurist
M W Pearson
A G Rice
G L Schade

MIDDLESEX EAST

J H Blaisdell
C W De Wolf
Richard Dutton
E H Halligan
J H Kerrigan
L L MacLachlan
M J Quinn
R. R. Stratton
J M Wilcox

MIDDLESEX NORTH

H R. Coburn
D J Ellison
A R. Gardner
W H Sherman
M A Tighe

MIDDLESEX SOUTH

C F Atwood
E W Barron
Harris Bass
J M Baty
S M Biddle
E H Bigelow
W O Blanchard
G F H Bowers
Madeline R Brown
R W Buck
E J Butler
J F Casey
B F Conley
H F Day
J G Downing
C W Finnerly

F W Gay
H W Godfrey
Ebot Hubbard, Jr
F R Joutet
E E Kattwinkel
A A Levi
F P Lowry
A N Makechnie
J C Merriam
C E. Mongan
G M Morrison
J P Nelligan
Dwight O'Hara
L G Paul
S H Remick
Max Ritvo
E F Sewall
A B Toppin
B M Wein
M W White
Hovhannes Zovickian

NORFOLK

Carl Bearse
Arthur Berk
M I Berman
L I Curran
William Dameshek
F P Denny
Albert Ehrenfried
Morris Frank
Susannah Friedman
J B Hall

R J Heffernan
I R Jankelson
C J Kickham
E L Kickham
D S Luce
T F P Lyons
F P McCarthy
R T Monroe
F J Moran
Hymen Morrison
M W O'Connell
S A Robins
S M Saltz
Kathleyn S Snow
M H Spellman
W J Walton
N A Welch

NORFOLK SOUTH

F W Crawford
D B Reardon
H A Robinson
W L Sargent

PLYMOUTH

G A Buckley
P H Leavitt
C D McCann
G A Moore
D W Pope
W H Pulsifer

SUFFOLK

H L Albright
A W Allen

H L Blumgart
W B Breed
W J Brickley
W E Browne
H M Clute
R L DeNormandie
N W Faxon
G B Fenwick
Reginald Fitz
Channing Frothingham
Joseph Garland
John Homans
A A Horner
H A Kelly
R I Lee
C C Lund
W J Mixtur
Donald Munro
H L Musgrave
H F Newton
R N Nye
F R Ober
J P O'Hare
L E Parkins
L E Phaneuf
Helen S Putman
W H Robey
E F Timmins

S N Vose
Shields Warren
Conrad Wesselhoeft

WORCESTER

Gordon Berry
W P Bowers
L R Bragg
P H Cook
G A Dix
E B Emerson
John Fallon
L M Felton
E L Hunt
J C McCann
R S Perkins
W C Seelye
C A Sparrow
J J Tegelberg
G C. Tully
R J Ward
F H Washburn

WORCESTER NORTH

E A Adams
H D Bone
C B Gay
B P Sweeney

APPENDIX NO 2

REPORT OF THE EXECUTIVE COMMITTEE

The Executive Committee held two meetings during the summer, a special meeting on July 10, 1942, and a regular meeting on August 26, 1942.

The special meeting was called by the president Dr. George Leonard Schadt, in consequence of a letter which he had received from Dr. Frank H. Lahey, chairman of the Directing Board of the Procurement and Assignment Service. This letter was by way of answer to the resolution offered by Dr. Reginald Fitz and adopted May 26, 1942, by the Massachusetts Medical Society at its annual meeting.

The Council will remember that those who had to do with supplying medical officers for the armed forces were greatly troubled by the fact that there was in this state a very considerable pool of licensed doctors who by reason of their school affiliations were ineligible for commissions in the medical corps of the armed forces.

The Massachusetts Medical Society, in adopting Dr. Fitz's resolution, memorialized the Surgeon General of the Army, the Directing Board of the Procurement and Assignment Service and others for the purpose of having the above ruling modified so as to make the members of this pool eligible for commissions under certain circumstances, which circumstances were set forth in the resolution.

We received acknowledgment of the receipt of this resolution from the Procurement and Assignment Service and from Surgeon General Magee. The Surgeon General's reply was received on June 15, 1942. In this letter he set forth four conditions under which the doctors in question would be accepted as applicants for commissions in the Medical Corps of the Army. One of these circumstances involved membership in the Massachusetts Medical Society. As these men had not been in practice for the necessary five years and consequently were not eligible

to apply for membership in our organization, the Surgeon General's letter did not solve the problem.

Dr. Lahey's letter, the reason for this special meeting, submitted a proposition in which the Surgeon General was reported to have concurred. This proposition involved an amendment to our by-laws. The Executive Committee, while expressing its every desire to be of service, felt that the acceptance of the proposition submitted involved the lowering of the standards of the Massachusetts Medical Society and that, furthermore, such a sacrifice would be without purpose inasmuch as any amendment to our by-laws could be ratified only at our annual meeting in May, 1943—certainly a too distant date to be of use in meeting what was at that time represented as an emergency.

Dr. Lahey was acquainted with the viewpoint of the Executive Committee.

On July 22, 1942, our office was in receipt of a letter from Dr. Lahey in which he enclosed a photostatic copy of a letter which he had received from Lt. Col. Lull, assistant to the Surgeon General. Colonel Lull's letter indicated that the Executive Committee's acts at its special meeting had come to the Surgeon General's attention. I will quote two paragraphs from this letter which refer to graduates of a certain medical school not on the approved list.

If these physicians meet the other qualifications, and have been practicing *less than five years*, the Surgeon General will accept a statement from the secretary of the county or district society to the effect that they are engaged in the ethical practice of medicine, and would be eligible for membership in the Society, except for the fact that they have been in practice less than five years.

The physicians who have been in practice for over five years, and who are not members of their district societies, will be denied commissions.

The President and Secretary, being satisfied that they understood the feeling of the Executive Committee in this matter, were somewhat troubled by the language which reads "and would be eligible for membership in the Society, except for the fact that they have been in practice less than five years." We suggested to the Surgeon General that this language be changed so as to read, "... be eligible to apply for membership in the Society. . . ."

The significance of such a change was not apparent to the Surgeon General, and there was further correspondence. This finally took the form of a statement from us to him as to how we felt we might be of help in this matter. We enclosed a form which we would direct the district secretaries to execute when presented by the applicant for a commission. Lt. Col. Lull suggested one very slight change in the form. This change has been made. The final form agreed upon is now on the screen [see page 744]. This form will be made part of the papers which the graduate of an unapproved school must have executed when applying for a commission in the Medical Corps of the United States Army.

As time was of the essence in this matter, a letter enclosing a copy of the form has already been sent to each district secretary asking him to evaluate the applicant from the standpoint of the circumstances outlined in the form. This is not a very great chore in the ordinary sized districts. In the larger ones, it may be necessary to set up some simple machinery to aid the secretary in arriving at the proper conclusion with regard to the individual applicant. The method, we are sure, may be safely left in the individual district.

No report on this matter would be complete without acknowledging the help received from Dr. Lahey, Dr. Fitz and Lt. Col. Marble. The Executive Committee hereby acknowledges with thanks that help. In the name of the Massachusetts Medical Society we have written the Surgeon General thanking him for this opportunity to serve.

The Executive Committee has approved of the method pursued and the conclusion arrived at in this matter.

The Executive Committee, acting on the recommendations of the Committee on Membership, has

- (1) Restored the following physicians to membership provided all their obligations to the Society are discharged within one month:

Gaspard M. Garoyan, Belmont
Lt. Col. Frank E. Lewis, Nantucket
Hugh B. Roney, Pittsfield
H. Sinclair Tait, Palmer

- (2) Denied the request of Dr. John F. McDonald that he be restored to membership.
- (3) Permitted Dr. Albert B. Ferguson to change his membership from Norfolk to Plymouth without changing his place of residence.

The Executive Committee was greatly impressed by the excellence of the report offered by Dr. Channing Simmons in the matter of his survey of the state-aided cancer clinics. This report has been sent to each councilor, together with the report of the Committee on Cancer, Dr. Shields Warren, chairman. The recommendations contained in this latter report were approved by the committee.

The Executive Committee reviewed the report of the Committee on Public Relations, Dr. Elmer S. Bagnall, secretary, and approved of the recommendation contained therein.

The committee reviewed the report of the Committee Appointed to Confer with the Massachusetts Hospital Association, Dr. Walter G. Phippen, chairman. The committee approves of the recommendations contained therein.

A letter from Mrs. John L. Bauer, presented to the Council at its annual meeting and referred to the Executive Committee, was laid on the table. This letter had to do with the formation in Massachusetts of a ladies' auxiliary to the American Medical Association.

Action on the suggestion of Dr. Frank R. Ober that two delegates be appointed to the annual meeting of the Associated State Postgraduate Committees was postponed.

The committee was in receipt of a letter from Dr. Dwight O'Hara, chairman of the Committee Appointed to Study the Practice of Medicine, asking for the discontinuance of this committee. The Executive Committee so recommends.

A letter was received from Dr. Henry R. Viets requesting that the Committee on Army Medical Library and Museum be discontinued. The Executive Committee so recommended.

Dr. Leroy E. Parkins suggested by letter that the Council of the Massachusetts Medical Society request the American Medical Association to change the place of its annual meeting from San Francisco to some city in the Middle West. The committee voted to lay this communication on the table.

The Executive Committee took notice of a resolution adopted at Atlantic City, June, 1942, by the House of Delegates of the American Medical Association, endorsing the work of the National Physicians Committee for the Extension of Medical Care. The Executive Committee voted to endorse the work of this committee and to recom-

mend that the Council of the Massachusetts Medical Society do likewise

The Executive Committee was aware that the calling of many doctors into the armed service was putting a severe strain on the time and efforts of those remaining at home

A summary of a plan intended to inform the public of the necessity of conserving doctors' time and energies was offered by the Yankee Network. The committee, having in mind the dwindling income of the Society consequent of the war, voted to decline the acceptance of this plan

Dr W Richard Ohler and others proposed that the Massachusetts Medical Society, in co-operation with Harvard, Tufts and Boston University Medical schools, sponsor a program of postgraduate instruction for the medical officers of the Army and Navy on active duty within the confines of Massachusetts. Preliminary conversations indicated that the schools, the Army and Navy were willing to participate in such a program

The committee voted to recommend to the Council that the Massachusetts Medical Society enter into such a program and that the President be authorized to appoint a committee of five to represent the Society in such joint sponsorship

Certain ad interim appointments, which will be offered by the President later in the meeting, were approved by the Executive Committee.

MICHAEL A TIGHE *Secretary*

APPENDIX NO 3

REPORT OF THE COMMITTEE ON ARRANGEMENTS

After a conference with the president and secretary of the Society, the Committee on Arrangements held a meeting at which it was decided to hold the next annual meeting on Tuesday and Wednesday, May 18 and 19, 1943, with the annual meeting of the Council on the evening of May 17. The Council, at its meeting last May, chose the meeting place as Springfield

Your committee anticipates that the 1943 meeting of the Society will be smaller in numbers and in exhibits than for the past few years, owing to gasoline rationing, to the fact that so many of our members have joined the armed forces and to other wartime conditions. For this reason we believe that the entire meeting can and should be held in the Hotel Kimball rather than in the Municipal Auditorium as it was the last time we visited Springfield

GORDON M MORRISON, *Chairman*

APPENDIX NO 4

REPORT OF THE COMMITTEE ON MEDICAL EDUCATION

At the request of the Executive Committee on June 24, 1942, we have investigated the nursing situation which has been produced by the war. We have consulted material from the American Nurses' Association and the hospital reports of the American Medical Association, and we have had conferences and correspondence with several hospital and nursing school executives and with the Army Nurses' Corps. These data impress us as requiring further study. The problem is complicated. It seemed best to ask your permission to accept a preliminary report today and to render a final statement at the next meeting

The sense of the following conclusions has been accepted unanimously by the committee

(1) The armed forces have asked for 60,000 registered graduate nurses, single, under forty five years of age and in good physical condition. Figures show that this need can be met, for in 1941 a national nurses inventory found 75,000 to 80,000 qualified women, and nursing schools will graduate 15,000 to 20,000 more this year. However, Army authorities have stated that they have had difficulty in getting nurses to sign up. We recommend, therefore, the closest possible co-operation between the Army Nurses Corps and the hospital executives and nursing school executives with a view to impressing on nurses who are qualified that it is their duty to join. It may be advisable to establish a nurses' procurement and assignment office to allocate them fairly. Perhaps the Army might be persuaded to accept certain married nurses, for marriage has not been a bar to the WAACs and WAVES

(2) The loss of so many nurses to the armed forces will create a serious shortage of nurses available for civilian needs. It has already done so. However, it is our considered judgment that at the present time there is no necessity for lowering the educational and training standards for graduate nurses, to speed up production. If the emergency increases, the possibility of some modification should be entertained. This would require changes in legislation in nursing registration regarding each of the forty-eight states

(3) Auxiliary nurses can be developed to meet the present situation. The Red Cross nurses' aides are important. They are for the most part mature women, they are taught quickly, and they have rendered excellent services already. Some five hundred centers are training them throughout the country. Perhaps 20,000 of the hoped for 100,000 have received certificates. The program is heartily endorsed. Other less voluntary services should be explored. For example, inactive graduate nurses who cannot return to full duty might be given part time work.

(4) The attendant nurse is worthy of far more consideration than she has received. Her course is only twelve to eighteen months long, and her educational requirements are not so great as those for the graduate nurse. Yet she is trained to do the jobs which are not emphasized in regular schools or for which the graduate nurse usually shows little aptitude—namely, the care of patients in their homes and the care of chronic illness. Therefore she is just the nurse to be relied on for rapid development and for tasks imposed by civilian disaster. It is recommended that the American Nurses' Association, hospital executives and physicians recognize her value explicitly and do all in their power to raise her morale. It is also desirable that government agencies utilize her wherever possible, as in veterans' hospitals and other chronic hospitals for chronic diseases

A campaign should be begun at once to train large numbers of attendants. This can be done without delay and with little cost if applicants can be attracted. The Household Nursing Association is running at only about 50 per cent of its capacity, it could double its capacity by using its eight affiliated hospitals more fully. There are 7 other attendant nursing schools in this state. More could be established if all the accredited small hospitals were engaged

It has been suggested that attendant nursing schools be formed in large hospitals alongside their regular nursing schools. This suggestion is opposed by the great majority of nursing educators and hospital administrators, and by

attendant nursing educators themselves. We believe that the experiment is not necessary and is not feasible because the two types of training are so different in objectives and in material required. Nevertheless it is being tried at the Beverly Hospital at the request of Mr. Frederick Ayer. The results will be instructive.

ROBERT T. MONROE, *Chairman*

APPENDIX NO. 5

REPORT OF THE COMMITTEE ON PUBLIC RELATIONS

The Committee on Public Relations has had a conference with Mrs. Emma Tousant, chairman of the Industrial Accident Board, concerning hospitalized beneficiaries of the Act. Mrs. Tousant believes that too often these patients do not get early and adequate care. She has conferred with insurance representatives, and they favor a gentleman's agreement to take care of the situation, rather than new legislation.

Preliminary discussion makes it apparent that there are problems that might be corrected by a meeting of minds. Your committee recommends that the President be authorized to appoint a subcommittee (not necessarily limited to the membership of the Committee on Public Relations) to confer with the newly appointed Medical Advisory Committee of the Industrial Accident Board, to see what should and can be done to improve certain aspects of the medical administration of the Act, particularly those related to hospitalized cases.

E. S. BAGNALL, *Secretary*

APPENDIX NO. 6

REPORT OF THE COMMITTEE CONCERNED WITH PREPAYMENT MEDICAL-CARE COSTS INSURANCE

The present opportunity is taken to make a report of progress concerning Massachusetts Medical Service. I should like to establish at this time the precedent of the president of the corporation making periodic reports to the Council on the progress of the Service. There are, furthermore, two other points at which intimate contact may be maintained between the profession and the corporation—first, the president can keep in touch with the districts by periodic meetings with the chairmen of the local professional-service committees and, second, the five physician members of the Board of Directors can sit at intervals with the members of the corporation (the Executive Committee of the Council) and thus be kept alert to the reactions of the physicians of the State. The maintenance of these close contacts will serve to maintain a proper understanding between the various groups involved in this venture.

It might be of interest to you to learn the fate of the resolution adopted by this group at its annual meeting relative to the principle of medical-service contracts. The resolution was presented and ably carried to the House of Delegates of the American Medical Association by your delegates, being presented on the floor by Dr. Mongan. With some slight change of wording it was adopted by the House of Delegates. Favorable comment on this action has appeared several times during the past few months in national publications interested in such problems.

It would be well at this time to take note of our indebtedness and express our appreciation to the lay members of the Board of Directors. Through the summer

months they have met several times in an effort to bring this endeavor to culmination. We are also indebted to the physicians who sat in the various committees which completed the necessary actions required to start the program. Particularly should we express our indebtedness to Dr. Nye and his associates on the staff of the *New England Journal of Medicine* for their whole-hearted co-operation in carrying information on the development of the program to the profession during the summer.

Very briefly I now report to you the actions that have been taken as a result of the several recommendations adopted by you on February 4, 1942. With reference to two recommendations,—one establishing the income levels of eligibility for service contracts as contrasted to indemnity contracts, and the other establishing the principle of developing a complete medical-care program through partial coverage contracts,—the Board of Directors voted approval of both these basic principles. With regard to the privilege asked to hire the services of an actuary, we did not find such a step necessary. Ample advice and help was forthcoming from Mr. Cleary, the actuary in the State Department of Insurance. The supplementary recommendation that empowered the Committee on Public Relations, the Executive Committee of the Council and additional appointees to review and establish the fee schedule and contracts was carried out by a summer meeting of this group. Two other recommendations—the first with reference to the selection of a director and the second relating to the establishment of a fund of \$25,000 by the Society—have been acted on. It is the opinion of the corporation that the financial requirements established by the Department of Insurance render it inadvisable at this time to employ full-time salaried agents. For the present, medical matters should be handled by voluntary committees of the Society. Business and administrative matters must be handled on a contract basis through the offices and agents of the Blue Cross. The financial requirements established by the Department of Insurance make no other course possible. What the future holds, so far as the relation of the two corporations is concerned, must evolve on the basis of experience. The remaining recommendation relates to the contractual relation between the Blue Cross and Massachusetts Medical Service. A carefully drawn contract supervised by the Department of Insurance safeguards the independent identity of the two corporations, and establishes the basis for the distribution of costs between the two corporations. It provides for the issuance of each corporation's contracts separately as well as jointly. The contract is renewable yearly.

It might prove of interest to you to have a brief report of the meetings that have carried this program into effect. As you will recall, prior to the annual meeting of the Society last spring, the Board of Directors of the corporation met and completed all necessary papers required to procure a charter. The charter was granted at the time of the annual meeting. At a subsequent meeting of the Board, in June, officers were elected, committees established, and approval voted of the general program as outlined by the Society. In July the Executive Committee of the corporation met with the actuary of the Department of Insurance, and the whole problem of the premium structure was thoroughly studied and decisions made. In August all basic contracts were studied by the Board and prepared for submission to the Department of Insurance. Following this, there were lengthy discussions with the representatives of the Department of Insurance, as a result of which the contracts were rewritten many times

until they satisfactorily conformed with all the department's requirements. This has been one unavoidable factor in delaying the start of the program. When all documents were in acceptable form, they were presented to the Executive Committee of the corporation for approval. Finally, in early September, the Commissioner of Insurance signed approval of all the documents and the program was launched. Since that time our whole endeavor has been to bring information to the physicians and solicit their enrollment as participating physicians. It is essential that a sufficient number of doctors be enrolled in any given area before sale of the contract to the public in that area will be justified.

I should like to show you now the organizational arrangement of Massachusetts Medical Service, so that you

Next to the left, is the Interlocking Services Committee, composed of two members from Massachusetts Medical Service, two members from the Blue Cross and one member who sits on the boards of both corporations. Next, in the center, is the Executive Committee, which can be quickly called to handle such problems as demand immediate action and cannot await the regular meeting of the whole Board. Next to the left is the Financial Committee, which of course is of major importance in any corporate organization. Finally, at the extreme left, is the Central Professional Service Committee, also required by the by-laws, which will be the effective group for introducing, for consideration by the Board of Directors, expert, studied, accurate reports on vital medical matters which will be assured support by the partici-

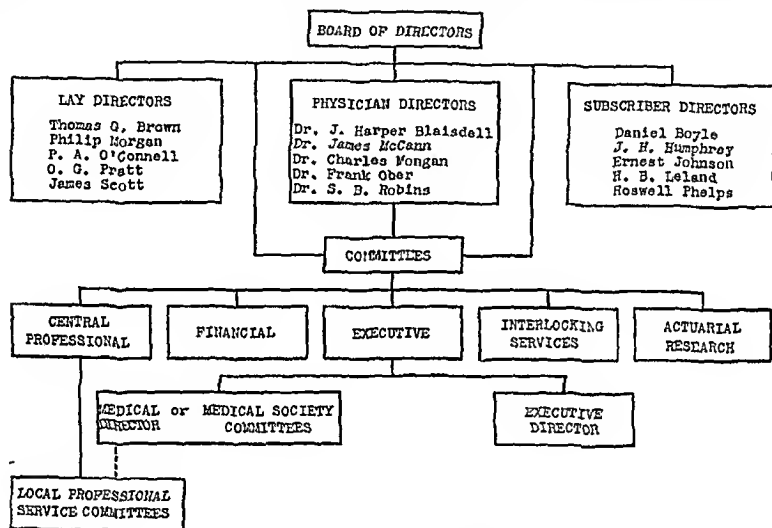


FIGURE 1 Committee Organization

may understand how the by-laws that you adopted will be put into practical effect. Figure 1 shows the manner in which the Board of Directors has been organized into subcommittees, and the method of contact between the profession and the Board. The single block at the head represents the Board of Directors, the effective managers of the corporation. The next line of blocks indicates the membership of the three component groups in the Board—the lay, the medical and the subscriber representatives. The personnel of these groups has been publicized in the *Journal* and in the press so that you are quite familiar with these names. The next single block—committees—indicates the breakdown of this whole group into effective functional units, which can carry out the many and varied tasks of such a managerial group. In the next row of blocks are the five functional committees established within the Board. At the extreme right is the Actuarial Research Committee, the establishment of which was required in our by-laws. The Insurance Commissioner believes that this should be an extremely acute and important committee in guiding the future development of the cor-

poration (without which there would be no corporation). This will guard against hasty unstudied action in significant medical matters, which, if taken even inadvertently, might have a violently disruptive effect on the affairs of the corporation from withdrawals of participating physicians. In the early organizational work, this mode of approach has functioned effectively and efficiently. In the next line of blocks are the effective day by day administrative units of such an organization. At the extreme right is the executive director with, of course, his entire administrative office force, which works under his direction. At the left is the medical administration, either a medical director or voluntary medical society committees. The restrictive financial requirements of the State Department of Insurance compel us to initiate our venture through the medium of voluntary medical society committees. Furthermore, some of the already existing plans now state that in the early period of organization it is preferable to start with voluntary committees rather than with a medical director. The early financial problems are difficult and, with our local re-

quirements, are prohibitive of paying a medical director for some time to come. In the last block are the local professional service committees, one in each district medical society. Direct contact is maintained between the local groups and the Board through both the Central Professional Service Committee and the medical director or the medical-society committees.

Table 1 indicates the allotment of the personnel of the Board into the committee positions. Dr. Frank R. Ober, with an invaluable background of medical-society activi-

tors to meet periodically with the members of the corporation (the Executive Committee of the Council). Contact with the physicians locally in their districts is of equal importance, and this is achieved by the interrelation of the Central Professional Service Committee and the eighteen local professional service committees. Practically, it will probably be desirable for the president of the corporation to meet periodically with the chairmen of the local professional service committees. These arrangements and contacts minimize disruptive misunderstandings, and ef-

TABLE 1. *Committee Membership.*

CENTRAL PROFESSIONAL	FINANCE	EXECUTIVE	INTERLOCKING SERVICES	ACTUARIAL RESEARCH
Dr. Frank R. Ober, chairman Dr. J. Harper Blaisdell Dr. Charles E. Mongan Dr. Samuel A. Robins One layman (rotating)	Thomas G. Brown, chairman Dr. Charles E. Mongan James Y. Scott Daniel J. Boyle	Dr. James C. McCann, chairman Philip M. Morgan Dr. Frank R. Ober Harold B. Leland P. A. O'Connell	Dr. J. Harper Blaisdell, chairman Oliver G. Pratt J. H. Humphrey Two Blue Cross representatives George Putnam and Dr. Nathaniel W. Faxon	Roswell Phelps, chairman Dr. Samuel A. Robins Ernest A. Johnson

ties, is chairman of the Central Professional Service Committee. Mr. Thomas G. Brown, banker, is chairman of the Finance Committee. Mr. Roswell Phelps, director of statistics, State Department of Labor and Industry, is chairman of the Actuarial Research Committee. Dr. J. Harper Blaisdell, a member of the boards of both the Blue Shield and the Blue Cross, is chairman of the Interlocking Services Committee. We are fortunate to have as members of that committee Mr. Putnam, president of the Blue Cross, and Dr. Nathaniel W. Faxon, whose leadership has been outstanding in both medical and hospital affairs.

It is important, I believe, that you visualize now the functional arrangement of the entire organization which you have created. This is, of course, related to the appointment of committees from the medical group, which has been approved of by the Executive Committee of the Board of Directors. Figure 2 outlines the tentative functional plans. In the first line of blocks are represented two vital factors in the organization. There is the Council, the true representative body of the Society, which has fostered, approved and created Massachusetts Medical Service. It has established the personnel of the Executive Committee of the Council as the voting members of the corporation. The fact that these members of the corporation are at the same time members of the Council assures close and intimate contact with the medical profession. In the first line also is the broadly representative Board of Directors, elected to act as the managers of the corporation by the members of the corporation (the Executive Committee of the Council). Drawn down from these in the second row of blocks is the Central Professional Service Committee, which is empowered to initiate action within the Board of Directors on vital medical matters. These men, functioning as the representatives of the profession in the Board, must be keenly alert to the sentiment of the profession in these matters, to preserve the support and the participation of the physicians throughout the State. It is important that these representatives keep in intimate contact with the central representatives of the physicians and with the local medical groups. The first is accomplished by the requirement that action on vital medical matters be reported to the members of the corporation (Executive Committee of the Council) thirty days prior to action. The members, in close contact with the Council, may then send resolutions and recommendations back to these five physician directors. Practically, it will probably be desirable for these five physician direc-

fectually bind the whole profession together in support of this important endeavor.

Carrying out the day-by-day administrative work of the corporation entails activities in two distinct planes. One is the purely business administrative plane, and this will be carried out by the Blue Cross office force on a contractual basis; the Blue Cross will function as our salaried agent, and the medical corporation will pay its proportionate share of expenses. The second plane might be referred to as the medical-relations plane. All the remaining blocks refer to this segment of activity. Leading down from the Central Professional Service Committee, through which they will function, are medical advisory committees made up of voluntary committees from the medical society. The first two committees are the Medical Publicity Committee and the Medical Speakers Committee. In the interests of sound public relations with both the profession and the subscribers, it is important that the lay publicity agents be somewhat advised so that their methods will agree with professional practices. Anything that smacks of improper advertising or the bludgeoning of those physicians into participation who have honestly not yet made up their minds concerning the merits of the endeavor or that does not carry the distinct intentions of the profession to the public must be absolutely avoided. The second committee, the Medical Speakers Committee, has already been proved necessary by the innumerable requests for speakers. The third committee, the Medical Review Committee, is the profession's present substitute for a medical director. The four items listed below the committee block are problems that must occasionally be passed on by such a group. In the early stages of organization it is probably highly desirable that these matters should be passed on by a representative group of physicians, rather than by a single individual—a medical director. As experience stabilizes these problems they will disappear, and then they might be passed over to a medical director. In the early formative period it is possible that a medical director might be granted more power over these matters than the profession is as yet ready to delegate to one man. It seems advisable to pass these problems through the hands of a small medical review committee, let us say eight men. Probably they will be able to make a decision quickly on the vast majority of problems. For difficult technical problems they will have the Specialist Review Pool, made up of three members of each specialty. A particular technical problem in orthopedics they can pass

down quickly for decision to the three orthopedic surgeons, and such report as they receive back they can relay of physicians in the United States, and also all data obtained from the enrollment forms so far submitted to the

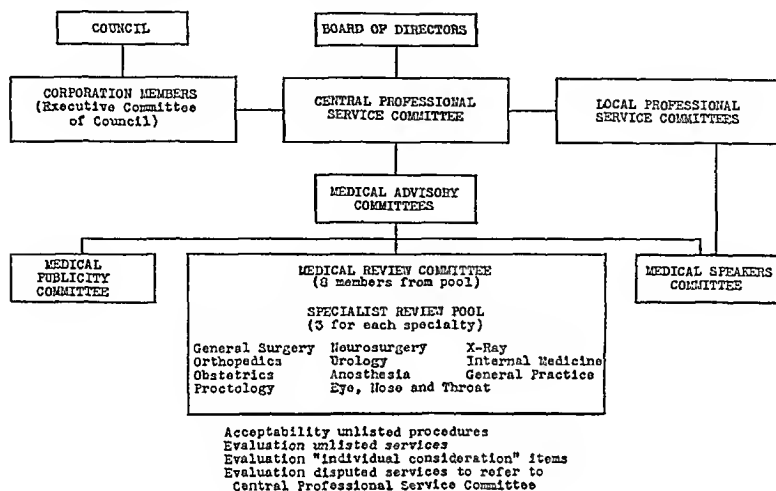


FIGURE 2 Functional Organization.

to the Central Professional Service Committee or to the administrative office for action. As the program broadens in coverage, additional specialist groups may be added to the pool.

For the present, this seems to be a rational method of procedure. With experience and time we shall undoubtedly find it advisable to modify this setup. However, in all matters—organization, contracts, schedules and so forth—I think we should feel that we have established a fair base from which to evolve gradually. Adjustments all along the line will prove inevitable. This, however, gives us a fair basis from which to proceed.

JAMES C. MCCANN, *Chairman*

APPENDIX NO. 7

REPORT OF THE MASSACHUSETTS STATE COMMITTEE, PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS

Since the last meeting of the Council, your committee has continued to work industriously. The medical military picture in Massachusetts has begun to clarify itself little by little and like any other picture has its good and bad sides.

Dr. J. J. Curley, of Leominster, one of the members of your committee, has resigned from it. He grew to feel that he could no longer be contented as a civilian and therefore applied for a commission. He is now a major in the Medical Corps of the Army. His services to your committee were invaluable and will be missed greatly but, on the other hand, he will make a splendid officer. His place has been taken by Dr. B. P. Sweeney, also of Leominster.

Within the past few weeks there have been sent to your committee figures dealing with the numerical distribution

Procurement and Assignment Service by Massachusetts doctors.

The age distribution of physicians in Massachusetts as of the year 1941 was as follows:

UNDER 35	35-44	45-54	55-64	65-69	70-74	75 AND OVER
2048 (27%)	1990 (26%)	1310 (17%)	1189 (15%)	550 (7%)	327 (4%)	298 (4%)

The enrollment forms submitted also yield the following information:

COUNTY OR DISTRICT	MEMBERSHIP OF MASSACHUSETTS MEDICAL SOCIETY (DISTRICT)	ENROLLMENT FORMS SUBMITTED (COUNTY)
Barnstable	63	55
Berkshire	135	140
Bristol	295	293
Essex	536	504
Franklin	53	42
Hampden	351	318
Hampshire	80	90
Middlesex	1357	894
Norfolk	1073	416
Plymouth	164	171
Suffolk	691	1947
Worcester	549	513
Miscellaneous		27
Total	5347	5440

These figures suggest that the majority of members of the Society have filled out their enrollment forms. That only 70 per cent of all the 7713 doctors in the State have done so, however, indicates that those who have been neglectful in supplying information concerning themselves still must be asked to fill out the forms at once. It would be helpful if all hospitals in the State reminded their regular and courtesy staff members to go to this trouble.

The discrepancy in figures from Middlesex, Norfolk and Suffolk is due to the fact that many members of Middlesex and Norfolk have offices in Boston and thus are listed

as belonging to Suffolk rather than to their proper district society.

Chief emphasis continues to be laid by both Army and Navy on the need for young medical officers. Since the commencement of its work your committee has been conscious of one serious handicap: we have declared "available" a great many young men after endeavoring to study each case individually and to be as fair and honest in our decision as to their classification as possible. Having declared a man "available," however, we soon learned that by no means all the individuals so designated had any intention of entering the armed forces.

It is a somewhat striking fact that random analysis of 100 enrollment forms sent in by doctors from all over the State shows that only one third put down Army or Navy as their first or second choice of how they hoped to serve the country during the national emergency and that a third were frank to admit they hoped to continue in private practice. These 100 forms included no names of men over thirty-five years of age. Most of these men are married and can claim dependents, thus under present Selective Service regulations they appear relatively safe from being drafted. About the only weapon with which to stimulate such men to make a patriotic gesture is that of public opinion. Fortunately, as time goes on, this becomes stronger; older physicians on hospital staffs and people in general are beginning to wonder audibly why certain young and healthy physicians are not in service. This sort of pressure is making itself felt. Thus each week we know of several newly appointed officers. The total number of members of the Massachusetts Medical Society who are commissioned has not been counted but it is fair to say that close to 1000 are now on active duty. We are informed that the enrollment from Massachusetts lags far behind that of most other states and that the need for officers from Massachusetts still is great.

We hear occasional grumbling that certain towns in the State have been depleted of young doctors. When such rumors are brought to our attention they are investigated at once through the district committees. There also has been sent us a list of men who put down as first or second choice on their enrollment forms a willingness to enter civil practice in other localities. Thus, so far there is little positive evidence of any real danger of medical depletion in any part of the State; in fact there still are a large number of young men in almost every district who should be encouraged to enter the armed forces rather than to remain behind. Machinery is now at hand to prevent or cure unnecessary depletion and we are endeavoring through Selective Service and the Medical Officers' Recruiting Board to perfect a workable method to stimulate young men to apply promptly for commissions who owe it to their country to do so.

The problem of industry in relation to Procurement and Assignment Service is beginning to assume larger significance than heretofore. We have received the names of all Massachusetts doctors who have expressed an interest in industrial medicine on their enrollment forms. This list is now being analyzed by the Committee on Industrial Health in co-operation with the Division of Occupational Hygiene of the State Department of Labor and Industry. Soon your committee will be in a position to assist the placing of men interested in industrial medicine and also to aid industries needing them to find properly qualified doctors.

The much debated question of the fate of the graduates of the substandard schools licensed to practice medicine

in Massachusetts has been solved. Your committee knows that an appreciable number of such doctors have received commissions in the Army irrespective of whether or not they were members of the Massachusetts Medical Society. The Surgeon General continues to decide in each instance how applications of this type shall be treated, and thus any direct action on our part is impossible.

On the whole, your committee believes that its work is progressing slowly but steadily along a well-ordered line. The committees in the several districts continue to work hard and conscientiously in their efforts to procure officers fairly, and also there is a fine spirit of co-operation on the part of hospitals, medical schools and various public-health officials.

HOWARD M. CLUTE
EDWARD L. KICKHAM
DWIGHT O'HARA
WALTER H. PULSIFER
B. P. SWEENEY
REGINALD FITZ, *Chairman*

APPENDIX NO. 8

REPORT OF THE COMMITTEE ON REHABILITATION

The last report of this committee to the Council of the Massachusetts Medical Society was dated May 18, 1942, and was approved by the Council at the last annual meeting. Since that time, no really important business has been transacted by this committee.

One member of the committee met with the Health Executive Committee of the Massachusetts Committee on Public Safety on June 25, 1942. Professor Curtis M. Hilliard, director of the Health Executive Committee, outlined in a general way the work which his committee had done. A considerable number of rehabilitation agents have been appointed and have reported some progress in their work. Ways and means of acquainting selectees rejected because of remediable defects or for other causes were discussed, and Professor Hilliard indicated that his committee would, so far as possible, take steps to inform those rejected what might be done to rehabilitate them.

Colonel Currier, of the Massachusetts Selective Service Headquarters, approved measures which had been attempted in this work of rehabilitation.

The federal government has done nothing further in this matter than was indicated in the report submitted at the annual meeting.

Your committee has, when called upon to do so, co-operated in every way with the Massachusetts Selective Service Headquarters in giving them such information as might reasonably and properly be given.

It seems now somewhat improbable that the federal government will, in the near future, undertake any extensive program of rehabilitation. If it is undertaken, the Massachusetts Medical Society will be ready to co-operate in an efficient manner with the federal or state government in this program.

RALPH M. CHAMBERS
JOHN FALLON
BENJAMIN F. ANDREWS
ARTHUR L. WATKINS
WILLIAM M. COLLINS
JAMES J. REGAN
WILLIAM E. BROWNE, *Chairman*

CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28461

PRESENTATION OF CASE

A forty-five year-old English machinist came to the hospital because of chills and back pain.

Sixteen days prior to admission the patient was awakened by a shaking chill, headache and a feeling of substernal oppression. He was vague about the duration of the chill, but it seemed to have lasted approximately two hours. He was not nauseated, did not vomit, had no pains and fell asleep promptly after the chill. The next day he felt well enough to get up but was weak and therefore did not go to work. On this day he noticed a small sore area on each knee about the region of the tibial tubercle, but could not account for their presence. He returned to work during the next two days. Four days after the initial symptoms he felt weak and after a bath again suffered with chills and fever. During this attack no feeling of substernal oppression developed. During the next four days he felt weak, anorectic and "not up to snuff." Eight days before entry he went to his physician, who told him that his liver and spleen were enlarged and advised him to have further studies made. He developed a dull aching nonradiating pain in the right scapular region, which continued to the time of admission but materially decreased in severity in the four days prior to admission.

It is of interest that the patient kept a dog, some rabbits and raised rats. He was bitten by one of the rats approximately two weeks prior to the onset of the present illness but the wound healed promptly. He had come to this country from Yorkshire, England, when nineteen years of age.

The family history was noncontributory.

Physical examination revealed a moderately well-developed and well-nourished man who appeared older than the stated age but did not appear acutely ill. The skin was sallow and seemed yellow. The sclerae had a suggestive yellow tint. On the left hand were the remains of two 1 cm. broken vesicles, which were said to have been mosquito bites. Several nontender lymph nodes, each approximately 1 cm. in size, were felt in the axillae and groin. Examination of the heart and lungs was negative. The midepigastrium seemed dis-

tended by a tumor mass, which was firm, did not pulsate and was not tender. It moved with respiratory excursions. The edge was felt six finger-breadths below the right costal margin. In the left upper quadrant was a separate "grapefruit-sized," freely movable, nontender mass extending from the costal margin to the umbilicus. However, this mass did not move with respirations. One observer believed the mass was attached to the umbilicus.

The blood pressure was 130 systolic, 90 diastolic. The temperature was 98°F, the pulse 80, and the respirations 20.

The examination of the blood revealed a red-cell count of 5,540,000 with a hemoglobin of 80 per cent, and a white-cell count of 16,450 with 75 per cent polymorphonuclears, 22 per cent lymphocytes, 1 per cent basophils and 1 per cent eosinophils. The urine and stool examinations were negative, as was the blood Hinton test. The nonprotein nitrogen was 23 mg. per 100 cc., and the icteric index 5 per cent. The van den Bergh test was negative. A bromsulfalein liver function test showed 5 per cent retention. An echinococcus complement-fixation test was slightly positive, and an echinococcus skin test was positive. A study of the gastric acidity revealed a normal amount of free acid.

An intravenous pyelogram outlined only the left kidney, and this seemed to be normal. A retrograde pyelogram was done to visualize the right kidney; this revealed no abnormalities except that the right ureter was curved outward. A barium meal showed that the stomach was elongated and markedly displaced to the left, owing to a large epigastric mass. In the recumbent position a second pressure defect was produced on the greater curvature by an orange sized mass lying below and to the left of the stomach. There was no intrinsic disease of the stomach or duodenum. A barium enema showed that the colon filled well, with some hesitation at the splenic flexure. The transverse colon was pushed well down to the pelvis by a 10 by 10 cm. movable mass. In the lateral view the mass could be seen posterior to the colon and pushing it forward, but not connected with it. A chest film was negative.

On the eleventh day after admission an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CHESTER M. JONES: I cannot recall having seen a protocol of a case that was so completely bewildering as this particular one. It says on the top of my copy, "For Differential Diagnosis." I am not sure I can present a differential diagnosis, but there are certain things here that are very interesting.

"He noticed a small sore area on each knee about the region of the tibial tubercle, but could not account for their presence." I think there are several red herrings and that is one of them. Whether I can keep clear of them remains to be seen.

This man had a sixteen-day story prior to admission, with an initial chill, fever and substernal oppression, weakness for four days, and then another chill and fever. We are not told what the height of the fever was. At the time of the last attack there was no substernal oppression. He must have felt sick and weak. Again, he had four days of weakness with indefinite intrathoracic symptoms and finally a decrease in severity of the subscapular ache or pain, not associated with cough or dyspnea and apparently not associated with any further manifestations of fever or chill, although we have to take that for granted from the history.

"He was bitten by one of the rats approximately two weeks prior to the present illness but the wound healed promptly." That is probably another red herring but it does raise questions.

Is Yorkshire a sheep country, Dr. Goulden?

DR. GOULDEN: Yes.

DR. JONES: "On the left hand were the remains of two 1-cm. broken vesicles, which were said to have been mosquito bites." A third red herring!

I suppose the left upper quadrant mass was thought by his physician to be spleen. The fact that it did not move on respiration is against its being spleen. The "attachment to the umbilicus" is a curious statement.

"The temperature was 98°F., the pulse 80, and the respirations 20." Those are very important facts, if they are facts, and if they continued the same throughout the course in the hospital. I assume he did not run a fever in the hospital. Is that right, Dr. Mallory?

DR. TRACY B. MALLORY: I find here that the temperature ranged between 100° and 102°F. rectally.

DR. JONES: There was a slight fever then, but without chills. It is of some importance, however, that there was no really abrupt temperature rise, no diurnal swing.

He had a definite leukocytosis and possibly a slight elevation of polymorphonuclear cells; the latter was not very striking, particularly with that degree of leukocytosis. The blood picture appears otherwise to have been normal.

There was no jaundice, and the suggestion on the part of the observer that the skin was sallow and the scleras icteric was not backed up by the presence of hyperbilirubinemia. The van den Bergh is an excellent check of the icteric index, and both were normal.

"An echinococcus skin test was positive." That is the fourth red herring. Whether that is the main fish or not, I do not know.

"An intravenous pyelogram outlined only the left kidney, and this seemed to be normal." The question is whether the right kidney was involved. I suppose they also wanted to see if there was displacement of the kidneys or ureters. At times this provides an excellent method of locating tumors in the abdomen.

At first glance the history seems to have no connection at all with the physical findings. Yet the physical findings were largely confirmed by careful x-ray studies, and showed a tumor outside the stomach and the urinary tract that displaced the stomach forward and to the left, and the colon forward and down. This seems to correspond with something that was felt in the left upper quadrant, which was called spleen by one man and a tumor attached to the umbilicus by another man, a tumor, moreover which did not move with respiration. There is no evidence of intrahepatic disease.

Finally, we have the perfectly flat statement, which I think cannot be doubted at all, that there was a positive echinococcus complement-fixation and skin test. Either this patient had a hydatid cyst or he did not. He might have had a hydatid cyst and a complication thereof or intercurrent disease with echinococcal disease that was purely coincidental, having nothing to do with the symptoms that brought the patient in. It can be pointed out, however, that echinococcal disease is symptomless for years, and also that 60 per cent of patients with echinococcal disease have cysts in the liver. This large mass on the right should have been liver until proved otherwise. I should say there is no reasonable doubt that the mass probably was the liver.

Symptoms arise from echinococcal disease only when there is a heavy liver or an accident, a rupture. It may involve other organs less frequently—the kidneys, the spleen and the peritoneal wall. It may involve the alimentary tract as well as the lungs. If there is an accident it draws the attention of the patient or his doctor to the disease. One accident of this type is the rupture of a cyst in the liver through the diaphragm into a bronchus, such as also occurs with liver abscess. That is ruled out here by the negative chest film. The hepatic cysts in echinococcal disease can rupture into the peritoneal cavity, into the retroperitoneal space and into the alimentary tract, and therefore it is entirely possible, if we disregard for the moment the onset of the initial symptoms, that this man has echinococcal disease, with a hydatid cyst of the liver, which probably ruptured into the peritoneal

cavity. The second mass, which was thought probably to be attached to the umbilicus, could be an inflammatory mass secondary to the spilling of the cyst contents. Another accident of echinococcal disease is suppuration of the cyst, but if such a patient has suppuration, he has the equivalent of a liver abscess, with more chills and fever and, by this time, other evidence of intrahepatic disease.

If the symptoms were not due to echinococcal disease, one has to consider a good many things ushered in by chills and fever and followed by a remission—in other words, a curious set of symptoms. He was bitten by a rat two weeks prior to the onset of symptoms. Could he have had rat-bite fever? Since the incubation period is fourteen days, the time is perfectly all right. Rat-bite fever runs a course of a few weeks. The fever may go down from a sharp peak for two or three days, with a second relapse higher than the first, and there may be a third, but the patient tends to get better all the time. I do not know how long the fever lasted in the first or second episode. There is frequently a skin rash in rat-bite fever. Also very frequently there is evidence of the rat bite. The liver and spleen are not particularly affected in rat-bite fever. This patient had a tremendous tumor, and if he had rat-bite fever, it is probable that he had another disease, which cannot be explained by that diagnosis. Furthermore, when the bite heals in rat-bite fever the healed wound subsequently breaks down and a scab is formed, which is rather sluggish in healing. There is no evidence of such a lesion. On the basis of his story the patient might have had spirochetal jaundice, but no jaundice was demonstrated at any time according to the laboratory data. Furthermore, in spirochetal jaundice there is not only fever but much more prostration, albuminuria of marked degree, and usually a slightly enlarged liver. This man had an enormous mass. He did not have spirochetal jaundice.

Could it be tularemia? He was taking care of rodents—rabbits and rats. Rabbits and rats carry tularemia. If he had had a bite from an infected rat he most certainly would have had a sluggish cutaneous ulcer, which would take weeks or months to heal. There was axillary adenopathy, but no streaking of the arm or local lesion. One could get an adenopathy without any evident wound, but this is uncommon. There was no involvement of the eyes, the ocular-glandular type of tularemia. There was nothing in the lungs. Furthermore the patient was not sick enough. The tularemia patient at the end of two weeks is very sick.

Could he have had typhus, which is associated with rats? The onset is not good for typhus. The clinical picture is associated with sudden onset, sudden headache and nausea out of proportion to anything else. At first, such patients are sicker than those with typhoid fever. The temperature is usually one of peaks and remissions. Furthermore, the big mass cannot be thus explained, and there was no skin rash.

I have no idea what this patient had unless it was echinococcal disease, with rupture of the cyst, probably into the peritoneal or retroperitoneal structures, forming a tumor mass, a cyst of the liver displacing the stomach, colon and right ureter, and a second tumor mass, which was not the spleen. It is obvious that he was explored because the mass was thought to be an echinococcal cyst.

My diagnosis is echinococcal disease.

Do you want to make a comment on the x-ray films, Dr. Holmes?

DR. GEORGE W. HOLMES: I am waiting for the signal.

DR. MALLORY: It might be amusing to put Dr. Holmes on the spot. As the record states, this patient was operated on and came back to the hospital ten years later with a feeling of discomfort in the left upper quadrant. After three days he felt a lump in the left upper quadrant and more x-ray films were taken.

DR. HOLMES: These films were taken ten years later?

DR. MALLORY: Yes.

DR. HOLMES: The stomach is displaced to the left, and the mass is on the right. The mass itself is dense and sharply defined and is perfectly consistent with a cyst. In these films the liver does not seem to be enlarged.

DR. MALLORY: Does the presence or absence of calcification in the wall of the chest mean anything?

DR. HOLMES: An echinococcal cyst should show some calcification of the wall. I suppose this fleck here is calcification, but there is not much and I cannot rule out some other kind of cyst. I think the story is consistent with echinococcal cyst.

DR. CASTLEMAN: Could it be a cyst of the pancreas?

DR. HOLMES: Yes. I am not attempting to say where it was or even whether it was in the abdominal cavity. It may have been in the pancreas. I do not believe it was in the spleen or kidney.

CLINICAL DIAGNOSIS

Echinococcal cyst.

DR. JONES'S DIAGNOSIS

Echinococcal cyst of liver, with possible rupture and secondary peritoneal involvement.

ANATOMICAL DIAGNOSIS

Echinococcal cysts of liver and gastrocolic omentum.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At the first operation two echinococcal cysts were found. One enormous cyst had replaced practically two thirds of the liver substance. The second was smaller and was located in the gastrocolic omentum. The smaller cyst was removed. It was quite impossible to resect the larger cyst, so it was opened and some hundreds of daughter cysts were evacuated. The inside of the cavity was formalinized, and the surgeon backed out.

As you have heard, the patient was perfectly well for ten intervening years. Then he came in again with another large cyst—this time in the retroperitoneal tissues above the pancreas. Again the cyst was too large to resect, and once again it was treated by evacuation and formalinization of the lining of the cyst. On the last occasion the surgeon made no note of any significantly sized cyst of the liver. Apparently the treatment had shrunk the cyst down very effectively. On this second occasion the patient left the hospital symptom free and apparently well for the time being. Nothing was ever found to explain the history and fever on the first admission. Neither cyst had perforated, but as soon as he was operated on the fever disappeared.

CASE 28462

PRESENTATION OF CASE

An eighteen-year-old boy came to the hospital because of post-traumatic pain and swelling of the right knee.

Approximately two months prior to admission while playing baseball he was struck below the right kneecap by a thrown baseball bat. There was some immediate pain below the knee, which forced him to stop playing. However, he was able to walk home without great difficulty. The next day the knee was painful and stiff, and felt best when partially flexed. The pain was moderately severe and rather constant, and did not radiate. One week later, slight swelling developed. Two weeks after injury, while riding in an auto-

mobile, he was thrown sharply against the edge of the steering wheel striking the right knee just above the kneecap. This was a painful blow, and soon after the swelling at the knee became prominent and the knee became very tender. After the second injury he noticed increased difficulty in extending the leg and in walking, owing to the discomfort incurred by flexing the leg. He had lost 17 pounds during this two months' illness.

The family and past histories were noncontributory.

Physical examination disclosed a slender, pale boy who appeared chronically ill. As he stood he could not bear all his weight on the right leg, and walking was very difficult owing to "weakness and pain in the right knee." Examination of the heart, lungs and abdomen was negative. There was a moderately soft, fluctuant swelling with a fluid wave about the right knee, extending from the level of the anterior tibial tubercle onto the lower third of the thigh. There was only slight fullness of the popliteal space. The patella was ballotable and was displaced laterally. There was increased local temperature over the knee, and tenderness to palpation along the medial aspect of the patella. The sharply demarcated edge of the quadriceps muscle was felt above the patella in the midline and anteriorly and medially over the femoral condyle. However, the patella moved slightly when the quadriceps femoris muscle was contracted. Knee flexion to a 95° angle was permitted.

The blood pressure was 110 systolic, 68 diastolic. The temperature was 101°F., the pulse 100, and the respirations 22.

Examination of the blood revealed a red-cell count of 4,700,000 with a hemoglobin of 80 per cent, and a white-cell count of 13,000 with 79 per cent polymorphonuclears, 9 per cent lymphocytes, 10 per cent mononuclears and 2 per cent eosinophils. Examination of the urine was normal except for occasional white cells and epithelial cells in the sediment. The blood Hinton test was negative. A tuberculin test with a 1:10,000 dilution was positive. The sedimentation rate was 2, 18, 22 and 38 mm. at fifteen-minute intervals.

An x-ray film of the right knee demonstrated a diffuse swelling in front of, below and above the patella, extending about one third the distance up the thigh and downward to the region of the tibial tubercle. The film of the chest was negative.

Soon after admission, the knee joint was aspirated, and 100 cc. of blood-tinged, rather viscous fluid was recovered. This was negative for aerobic and anaerobic bacteria. On the fourth day after

admission, a course of orally administered sulfadiazine was begun. A total of 78 gm. was administered during the succeeding seventeen days, without remarkable effect. The temperature continued to rise each evening to approximately 101°F ., and the pulse rate remained fast, varying usually between 90 and 115. During the course of sulfadiazine, the urine at times showed a $+$ test for albumin and occasional granular and hyaline casts, and on one occasion red blood cells were noted. No sulfadiazine crystals were found in the urine. The sulfadiazine level in the blood was not known to have exceeded 9.0 mg. per 100 cc. The fluid intake and output was satisfactory.

On the fifth day after admission the knee joint was again aspirated, and 50 cc. of thick, tenacious, bloody material was recovered. This was found to have a red-cell count of 36,000 and a white-cell count of 7600. In the differential count there were 48 per cent polymorphonuclears, 48 per cent monocytes and 4 per cent lymphocytes. Cultures for aerobic and anaerobic organisms were negative. Four days later the joint aspiration was repeated, and a similar material recovered. The red-cell count was 105,000, and the white-cell count 41,000 with 90 per cent polymorphonuclears, 3 per cent lymphocytes and 7 per cent monocytes. There was a fairly large amount of atypical mucin in the material. In the examination for mucin a large amount of precipitate formed but in small pieces, which did not cling to a stirring rod. The sugar of the joint fluid was 6 mg. per 100 cc., and at this time the fasting blood sugar was 82 mg. Three days later the joint fluid was bloody, thick and slimy, with a red-cell count of 33,000 and a white-cell count of 96,000, with 85 per cent polymorphonuclears, 14 per cent monocytes and 1 per cent lymphocytes. The fluid had a sugar content of 6 mg. per 100 cc., and at this time the fasting blood sugar was 98 mg.

An operation was performed twenty-nine days after admission.

DIFFERENTIAL DIAGNOSIS

DR. FRIEDRICH W. KLEMPERER: Mucin if precipitated with acetic acid normally forms a precipitate that is stringy and ropy. Mucin may be present in normal quantity, but may not show the typical precipitate with acetic acid. In this case one sees flocculation or sometimes just turbidity. This atypical behavior is due to depolymerization of mucin, which usually is a sign of infection, but may also be found in other kinds of arthritis.

Here we have an eighteen-year-old patient who sustained a definite injury to his knee. This was immediately followed by pain, but there were grad-

ually increasing swelling and disability following injury. He had a second injury two weeks later, which aggravated these symptoms but did not otherwise change the picture. During the two-month period following the onset of symptoms we know that the patient lost 17 pounds. Nothing is said in the history about constitutional symptoms or fever, but the remark in the examination on admission that the patient appeared chronically ill indicates that he must have had moderately severe constitutional symptoms, and probably fever. The description of the physical findings in the knee seems slightly confusing. There was undoubtedly a large effusion in the knee, and some periarticular swelling. I cannot make out where the edge of the quadriceps muscle was, but it was apparently held in transverse position. Whether this means more than soft-tissue swelling or whether there was some atrophy around the joint that made the muscle edge stand out more, I do not know. There was displacement of the patella, but it does not say to what degree. I assume that a large amount of fluid can displace the patella slightly. In the x-ray report nothing is mentioned about bone involvement, and the picture as described indicates an effusion and soft-tissue swelling.

DR. TRACY B. MALLORY: Here is a diagram that may help you.

DR. KLEMPERER: According to this diagram it does not seem as if the patella were displaced markedly.

May we see the x-rays?

DR. GEORGE W. HOLMES: I presume this film was taken of the chest to make certain that the patient did not have metastasis from some sort of tumor, and I should interpret the chest as essentially negative.

This film was taken to bring out the soft-tissue shadows about the knee. It is somewhat underexposed, whereas the other films were taken in the usual manner. I think we can be quite certain there is no disease of bone demonstrable by x-ray. They are very satisfactory films and are entirely negative.

DR. KLEMPERER: How much atrophy of the bone is there?

DR. HOLMES: Practically none. There is a tremendous amount of thickening of the soft tissue in front of the bone, and it is rather unusual in that it extends below the patella. An accumulation of fluid may extend up into the thigh but it is unusual; I do not know that I have ever seen it extend so far below the patella. The joint space might come down that far, but I cannot be sure that such is the case.

DR. KLEMPERER: He had a large effusion?

DR. HOLMES: He did. Another queer thing is the lack of demarcation between the tissues in that area. The swelling may have been due to edema, but ordinarily when there is fluid in the joint space, one can see details in the tissue.

DR. KLEMPERER: Traumatic arthritis is practically ruled out by the clinical story of weight loss, temperature and leukocytosis. Another very strong point against traumatic arthritis are the findings in the joint fluid. Traumatic effusions never contain a large number of white cells. The highest count we have had was 5800, the average being around 1000; furthermore, the polymorphonuclears never exceed 35 per cent. One never sees low sugar values in the fluids of traumatic arthritis. The mucin should have a good quality and precipitate in a typical manner. Of course there are other kinds of arthritis that can be precipitated by trauma, or the trauma might represent the localizing factor in infectious arthritis.

A tumor should be ruled out too. The history of fever, the constitutional symptoms and leukocytosis are not in favor of tumor. The same holds for the fluid findings. The fluid in a case of tumor resembles that of traumatic joint fluid unless the tumor is infected later. One never sees cell counts up to 100,000, with a predominance of leukocytes. Furthermore, in most cases the mucin precipitates well and the sugar is high. On the basis of the fluid, I am inclined to rule out tumor unless secondary infection supervened. The x-ray film might possibly be interpreted as showing a soft-tissue tumor, but I should think that it represents marked synovial swelling, with periarticular edema that obscures the details of a large effusion.

Rheumatoid arthritis usually presents an entirely different picture. The onset is preceded by prodromal symptoms, weight loss and general fatigability, of which we have no indication, and the joint involvement is usually polyarticular and symmetrical. However, 18 per cent of the cases in our series were atypical. The joint involvement may be monarticular at onset. The disease occasionally follows injury and may be accompanied by severe constitutional symptoms, fever and leukocytosis. Clinically, the picture could be this. The absence of bone involvement, the periarticular swelling and the effusion are consistent with rheumatoid arthritis. However, again on the basis of the fluid findings, I shall rule out rheumatoid arthritis. The white-cell count in rheumatoid arthritis ranges from 600 to 66,000, with an average of about 5000 to 10,000. The highest white-cell count in this case was 96,000, and only a small number of the leukocytes can be accounted for by blood that may have entered the joint during the tap. The polymorphonuclears in rheumatoid

arthritis vary from 5 to 95 per cent. One even more important finding is that, although the joint involvement was of short duration, eight or nine weeks, at the time of the joint tap, the aspirated fluid contained practically no glucose. We have never seen an early rheumatoid effusion with a low sugar. During the first few weeks the sugar in the fluid has about the same level as that in the blood. After six months we have seen it go down to something like 30 mg. per 100 cc., and only after a year is there an occasionally negative sugar, as in this case. This fluid finding indicates that rheumatoid arthritis is extremely unlikely.

This brings us down to the septic arthritides. The first is gonococcal arthritis. There is no history of genitourinary infection. Nothing is said about a primary focus, such as urethritis or prostatitis. There were no chills. The temperature was not high. The joint symptoms were not very acute. The joint was not red or extremely tender. The duration of the effusion in gonococcal infection usually does not last close to three months, as in this case. However, a low-grade infection might possibly produce a picture like this. Sterile joint fluid is often found in milder cases, when the organism has invaded the synovial membrane but not the joint cavity. However, these are rather avirulent cases and never show a cell count up to 100,000, and absence of sugar in the joint fluid. I should say if this were gonococcal arthritis it should show either a positive culture or the white-cell count would be less and the sugar higher. Septic arthritis due to pyogenic organisms, — staphylococcus, streptococcus or the pyocyaneus bacillus — is unlikely. There was no primary focus of infection, and no portal of entry to the joint is mentioned. The patient did not have chills, and the findings were not typical. The duration is too long for a septic joint. The patient either gets well or worse within two or three months.

The other organisms that might account for a monarticular arthritis should be mentioned. In a generalized meningococcal infection, arthritis might be the first symptom, but the nature of the fluid is against it.

I shall mention in passing the other diseases in which arthritis is a secondary feature of the general disease, such as pneumococcal infection, dysentery or typhoid fever, although I do not want to consider them seriously. Lymphogranuloma inguinale as the cause of arthritis almost always produces polyarticular involvement, and purulent fluid is never found, so far as I know. Syphilis is ruled out clinically as well as serologically.

This brings us to tuberculosis of the knee. The clinical history is consistent with tuberculosis.

Trauma is known to precipitate or determine the localization in tuberculous arthritis in about 50 per cent of the cases in some series. The slow progression of symptoms, the weight loss and the moderate temperature without chills are all consistent with tuberculosis. The physical findings about the knee are also typical. The large amount of synovial and periarticular swelling with atrophy of the muscles early in the game is characteristic. Large effusions are not frequently found but are possible. The absence of a pulmonary lesion is not very important. Only about half the patients show lung lesions, and from the tuberculin test we know that the patient must have had some previous tuberculous infection. The most significant finding is the character of the fluid. The atypical appearing mucin, the high cell count and the low sugar are very typical of tuberculous arthritis. In other kinds of arthritis the level of the sugar is usually in inverse proportion to the severity of the involvement and to the white-cell count in the joint fluid. However, in tuberculosis, relatively low counts with absent sugar are quite characteristically found. Of course, there is a somewhat puzzling variation in the fluid findings. In the first, the cell count was 7000, and then it continually went up so that the second was 30,000 and the last 96,000. This is unusual for tuberculosis, but it is also unusual for any other kind of arthritis. I am thinking of one possibility. This fluid was described as slimy, thick and tenacious, and in such turbid fluid the white cells occasionally clump and one cannot obtain a representative sample of fluid or an accurate cell count. Whether this was so, I do not know, but it is certainly a possibility. On account of the findings I am inclined to think that tuberculosis is the most likely cause of this patient's difficulties.

Of course in any kind of unusual joint disease undulant fever should be considered. This would be an atypical case, but the typical clinical picture is often lacking and frequently one does not find the leukopenia that is characteristic. The joint involvement is usually polyarticular and without objective signs. Severe signs like this are very unusual, and only a few cases have been described where just one joint was involved and pus was recovered from that joint. These cases are open to the question whether they really represent brucella infection, because the organism was found in none of them. Brucellosis is a possibility, although I think it is very unlikely.

I believe the operation performed on the twenty-ninth day was a biopsy, and I also think that tuberculosis was found in the synovial membrane.

DR. MALLORY: Have you anything to add to the question of tuberculosis, Dr. Holmes?

DR. HOLMES: The absence of any evidence of disease in the bone or joint cartilage is against tuberculosis, although the bone may be negative in cases of tuberculosis of the synovia. I do not see how we could rule that out.

CLINICAL DIAGNOSIS

Pyogenic infection of knee.

DR. KLEMPERER'S DIAGNOSIS

Tuberculosis of synovia of knee joint.

ANATOMICAL DIAGNOSIS

Tuberculous bursitis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: I see no member of the Orthopedic Service here to describe the operation. As Dr. Klemperer suggested, the operation was done for biopsy. I judge from the operative note that the surgeon, to his considerable surprise, found a cavity almost immediately after going through the skin. This cavity contained hemorrhagic material and was lined with a semicaseous surface. Biopsy from this wall showed tuberculosis. Further exploration showed that the cavity extended well up into the thigh beneath the quadriceps muscle, and that a fistulous tract extended downward lateral to the patella, which accounted for the swelling below the patella noted by Dr. Holmes. The surgeon did not open the knee joint but tapped it and obtained clear fluid. We have no certain evidence whether or not the knee joint was directly involved. In one of the various taps presumed to have been of the joint it was remarked that fluid was obtained after barely puncturing the skin. So it is possible that several of the fluids examined did not represent joint fluid but came from the inflamed bursa. However, the chemical findings led to the correct etiologic diagnosis whether the site of involvement was the joint or not.

DR. HOLMES: The homogeneous density of the joint in front should have made us suspicious.

DR. MALLORY: Certainly most of the infection was outside. I cannot say whether there was any in the joint or not.

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REHABILITATION AND PREHABILITATION

NINETY per cent of the youths from sixteen to twenty-four years of age in low-income families are in need of medical or dental care. Two thirds of the whole group, which is believed to be representative of some 12,000,000 American youths, are physically fit for any kind of work; one third of them are limited by health defects in what they can do. These figures, contained in a recent joint release of the United States Public Health Service and the National Youth Administration, are based on physical examinations of 150,000 out-of-school youths on work programs of the NYA. Despite the well-known fact that statistics are often misleading, such figures, as well as the data provided

by the Selective Service examinations, furnish food for thought.

In the first place, American youth, physically impoverished as it may be, is not so unhealthy as the large scale examinations of 1917 and of 1940-1942 have led many critics to believe. The standards used must be considered, and although impaired eyesight, certain degrees of dental caries and pronated feet must be classified as defects, they do not necessarily impair the health or interfere with physical vigor.

In the second place the discovery of true disease or of major defects and their subsequent treatment are of vast importance to the individual as well as to industry, to the war effort and to the tax-paying public, as are the discovery and correction of the remediable minor defects.

In the third place the physical examination itself is held up for review, to determine its effectiveness and its time-honored inadequacies and the changes in it that are necessary from time to time to make it fulfill the functions for which it is intended and with which it is credited.

Out of the Army examinations and rejections has come a new interest in an old word — rehabilitation. Those whom the military machine cannot immediately use must not be left discarded by the wayside. They must be listed, repaired and reclassified — made ready for future military service or for whatever service they can best be fitted into. The next step in the program is an anticipatory one: the finding, before they come of useful military or civil age, of those who require correction of defects, in order that they may not be later rejected. This is prehabilitation, and it is gradually but surely becoming a potent factor in the readying of the manpower of the Nation.

THE NEWS

THE first number of a new bulletin from the Massachusetts General Hospital, entitled *The News* and dated October, 1942, has been received. This pamphlet is really a continuation of the *Massachusetts General Hospital Bulletin*, established in 1913,

which was subsequently interrupted by the activities of World War I. Publication was resumed in 1919, only to be suspended in 1926. Again, in 1928, a new bulletin was started, but this was given up during the financial depression of 1932. Thus a spark has been kept alive, although intermittently the flame has almost died out.

There apparently is a need for some medium to spread the news about a great hospital, much of which cannot find its way into the annual report or, if it does so, is too late to have anything but historical value. News quickly becomes uninteresting if allowed to lie too long on the shelf. The new publication is therefore welcome, particularly at this time, for it brings to one's attention the splendid effort made by the voluntarily supported hospitals toward the war. In the present number are not only a photograph and data concerning the present Massachusetts General Hospital unit, the Sixth General Hospital, but also a long list of men who are serving in various branches of the armed forces.

MEDICAL EPONYM

SCHULLER-CHRISTIAN'S DISEASE

Professor Artur Schuller (b 1874), of Vienna, wrote a paper, "Ueber eigenartige Schadeldefekte im Jugendalter [Peculiar Skull Defects in Children]" which was published in *Fortschritte auf dem Gebiete der Röntgenstrahlen* (23:12-18, 1915). He described three cases, and a translation of his conclusion is as follows:

Each of these briefly outlined cases represents a noteworthy and extraordinarily uncommon condition. Common to all three is the fact that there were extensive defects in the skull that developed without pain and without any cerebral symptoms of any sort — practically without symptoms of any kind. Neither could there be discovered in these cases any of the recognized causes for such defects in the skull. Of interest, too, is the presence of a hypoplastic symptom complex in two of our cases, namely dystrophia adiposogenitalis in the first, and diabetes insipidus in the second. Finally, the relatively rapid disappearance of the defects, which was clearly perceptible by x-ray, constituted a noteworthy feature of the second and third cases. We suggest the name 'geographical skull' [*Landkarten schädel*] as a suitable term for the peculiar appearance of the x-ray defects that we have described.

Dr. Henry A. Christian (b 1876), Hersey Professor of the Theory and Practice of Physics, Harvard Medical School, described "Defects

in Membranous Bones, Exophthalmos and Diabetes Insipidus. An unusual syndrome of dystrophia" in the *Medical Clinics of North America* (3:849-871, 1920). After presenting a case and referring to those described by Schuller, he concludes:

A case is presented where, in a girl of five, there occurred the symptom-complex of very extensive defects in the skull bones, exophthalmos and diabetes insipidus. Only 2 other cases of this condition could be found in the literature. Diabetes insipidus suggests that the symptom complex is due to a disturbance of pituitary function. Both of the other 2 reported cases showed evidence of disturbed pituitary function.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING THE YEAR 1941

MEDICAL CAUSES (continued)

The previous two issues of the *Journal* have discussed the maternal deaths associated with heart disease and pneumonia. The following is a résumé of the remaining 8 deaths in the group allocated to medical causes.

Two of these were definitely associated with hypertension. The first case was that of a patient between three and four months pregnant who was admitted to the hospital unconscious. She was known to have had a high blood pressure for three years; in 1940 when she had a miscarriage at five and a half months, her blood pressure was 240 systolic, and 120 diastolic. Prior to entry she had suffered a cerebral hemorrhage with right hemiplegia and had a blood pressure of 250 systolic, 150 diastolic. An autopsy was performed. From the medical standpoint there is every argument against the occurrence of pregnancy in this case, for it definitely irritated the hypertension and caused the catastrophe.

The second case was that of a twenty-five-year-old woman, approximately five months along in her first pregnancy, who gave a history of repeated attacks of sore throats with cardiac involvement. She was hospitalized because of a blood pressure of 190 systolic, 120 diastolic, and signs of cardiac embarrassment. Digitalization improved the cardiac condition but in spite of this the kidneys shut down entirely; the nonprotein nitrogen varied from 34 to 55 mg. per 100 cc., and the urine showed a ++++ test for albumin and casts. She died undelivered of uremia. The comment made on the foregoing case applies

here. Neither of these patients should have been allowed to become pregnant, if one looks at it from a purely medical point of view, and in the event of pregnancy, abortion should have been advised.

There were two cases of meningitis. One of these was tuberculous in origin and occurred in a patient approximately five months pregnant. She was seen at home twice by her local physician and sent to the hospital practically moribund, with a stiff neck, a temperature of 104°F. and a pulse of 150. Death occurred forty-eight hours later. Although cultures and smears for the organism were negative, the diagnosis was based on the spinal-fluid findings. This patient died undelivered.

The second case of meningitis occurred in a patient who had had a normal delivery and was discharged on the tenth post-partum day. She returned one month later with the story that two days before entry she had been seized with a severe headache, which was followed by a stiff neck. Lumbar puncture revealed cloudy fluid, and 20 cc. of antimeningococcus serum was administered. Blood culture was positive for streptococcus, and death occurred two days after admission. This death had nothing whatsoever to do with the obstetric condition; it just happened to be co-existent.

The next 2 cases in this series were allocated to gastric ulcer. The first of these was a woman who was delivered normally at home of her fifth child. Four days after delivery she vomited blood and had tarry stools, and arrived at the hospital two days later in very poor condition. She was transfused, but death resulted from massive hemorrhage from the stomach. This was a most unfortunate catastrophe that had nothing to do specifically with the pregnancy.

The second patient was delivered by low forceps, when approximately eight months pregnant, of a stillborn infant. Vomiting had occurred a week before delivery, and death resulted from hemorrhage two days post partum. It is possible that the hemorrhage was due to an esophageal varix, but no autopsy was performed to confirm this. This case again has no particular association with pregnancy.

One death was due to ulcerative colitis. A patient who had had diarrhea for four or five weeks entered the hospital when about four months pregnant, a spontaneous miscarriage occurring four days after entry. She ran a septic temperature and died sixteen days after delivery, in spite of sulfonamide therapy. Autopsy revealed ulcerative colitis and generalized peritonitis; there was no apparent perforation of the bowel, but pneumoperitoneum

was discovered. Although there was no visible rupture of the uterus, there is some question whether instrumental interference with the pregnancy had been attempted.

The last of the deaths allocated to medical causes was due to pulmonary tuberculosis and occurred in a woman who was apparently seen for several months by her physician before tuberculosis was diagnosed. She reached the sanitarium practically moribund, and death occurred the day following the normal delivery of a stillborn infant. It is a sad commentary on medicine in Massachusetts that this case of tuberculosis could have run so serious a course before consultation was held or the diagnosis made.

WAR ACTIVITIES

CIVILIAN DEFENSE

EMERGENCY BASE HOSPITALS

The Medical Division of the United States Office of Civilian Defense, through its regional medical officers and the state chiefs of Emergency Medical Service, has now made emergency provision for the establishment of a chain of emergency base hospitals in the interior of all the coastal states. They will be activated only in the event of an enemy attack that necessitates the evacuation of coastal hospitals. Each base hospital will be related to the casualty receiving hospital that has been evacuated, and it is expected that the staff will be recruited largely from the parent institution.

To meet a sudden and unexpected crisis without delay, arrangements have been completed with state authorities for the prompt taking over of appropriate institutions in the interior of the state for this purpose and with local military establishments for the transportation of casualties and other hospitalized persons along appropriate lines of evacuation.

More than 150 hospitals in the coastal cities are in the process of organizing small affiliated units of physicians and surgeons, who will be prepared to staff the emergency base hospitals if they should be needed. These units are composed of the older members of the staff and those with physical disabilities that render them ineligible for military service, and of women physicians. The doctors comprising units are being commissioned in the inactive reserve of the United States Public Health Service so that, if called to duty, they may receive the rank, pay and allowances equivalent to those of an officer in the armed forces.

Dr. George Baehr, chief medical officer of the United States Office of Civilian Defense, states that the members of these affiliated hospital units will continue to remain on an inactive status for the duration of the war, unless an enemy attack in their region necessitates the transfer of casualties to protected sites in the interior. Their commissions may be terminated on their request six months after the end of the war, or sooner if approved by the Surgeon General. Such approval will be given in the event such officer desires active duty in the Army or Navy.

MISCELLANY

TUFTS COLLEGE MEDICAL SCHOOL

President Leonard Carmichael, of Tufts College has recently announced the gift of a tract of land in downtown Boston from Mr A Shapiro, of Brookline. The property, consisting of five buildings on Tyler Street was formerly owned by Denison House and adjoins property on Harrison Avenue recently purchased by the school. It is adjacent to the hospitals and dispensaries of the New England Medical Center, of which Tufts is the teaching base.

The land was purchased, according to Mr Shapiro so that there will be plenty of elbow room around the proposed three-quarter million-dollar medical building. President Carmichael said that the gift was prompted by the donor's appreciation of the rural medical extension program being developed by the Tufts faculty at the New England Medical Center, a project whereby many local communities in Maine were benefiting from the school's extension of laboratory and diagnostic services, training of local hospital technicians and assistance in organizing emergency medical protection such as a state wide network of civilian blood banks. The donor expressed hope that the gift would induce similar contributions from other laymen.

The President announced that well over half a million dollars has now been subscribed for the new building and efforts are being made to complete the fund so that the medical school, which is the principal training center for New England doctors, may build as soon as conditions permit.

NOTE

Professor Edwin J Cohn, head of the Department of Physical Chemistry at Harvard Medical School, recently delivered the third Alvarenga Prize Lecture before the College of Physicians of Philadelphia and the Philadelphia County Medical Society. The title was 'Plasma Proteins: Their properties and functions'.

CORRESPONDENCE

RACE, COLOR AND RELIGION

To the Editor In the recent exchange of correspondence over the industrial health questionnaires in the October 8 issue of the *Journal*, it is unfortunate that Dr O'Hara regarded the entire matter as 'ill-natured' and that Dr Muller allowed himself to be drawn into personal attack on Dr O'Hara. As a result, the real issue, which is an important one, was obscured.

The point is simply this: the question about race, color and religion is an old stand-by of those who subvert the principles of democracy by discrimination in employment or elsewhere. It is, no doubt, true—as Dr O'Hara maintains—that certain employers desire these data. But since they have absolutely no bearing upon medical ability, their only use would be as a discriminatory weapon. The selective service registration, which Dr O'Hara cites by way of analogy, requests information about color, height, weight, hair color and so forth purely for identification purposes and there is clearly no discriminatory intent. On the other hand it has been the policy of the United States Employment Service for some time to refuse this type of information to employers, and the latter if they hold war contracts, are expressly for-

bidden to discriminate against able workers for reasons of race, color or religion.

For these reasons the Committee on Industrial Health ought not to have made itself the agent for perpetuating unfair and un-American employment practices. Today, physicians of all racial and religious groups are entering the armed services, creating a serious problem of properly redistributing the remaining doctors to civilian needs. At such a time our country needs the right men in the right places, and we can ill afford the luxury of weeding out capable physicians on the basis of blood composition, skin pigmentation or church affiliation. Fortunately, doctors are so scarce now and industry so badly in need, that organized medicine could, if it wished, play an important role in breaking down these undemocratic practices of discrimination. May we suggest that the Massachusetts Medical Society handle this question as our government does and refuse prospective employers any information that could be used in a discriminatory fashion?

AVRAM GOLDSTEIN, H M S 44, Chairman
New England Region, Association of Internes and Medical Students

383 Longwood Avenue
Boston

* * *

Mr Goldstein's letter was referred to Dr O'Hara, chairman of the Committee on Industrial Health, Massachusetts Medical Society, whose reply was as follows:

To the Editor By the use of such words and phrases as 'questionnaire,' 'real issue,' subvert the principles of democracy, discrimination and unfair and un-American practices and by direct implication that the Massachusetts Medical Society somehow has prying motives that are beneath the dignity of our government, Mr Goldstein forces me to write again, much as I regret to ask for more of your space.

It is hard for me to believe that anyone who has seen our little registration form, or who knows the members of our committee, or is in any way familiar with the temper of the Council to whom the committee reports and is responsible can fail to be unimpressed with the nature of this correspondence, be it good or ill. I can assure Mr Goldstein and all those who habitually fear persecution and evil that our committee has no inquisitorial designs or desires. We do not care whether such persons register with us, but if they do, we shall earnestly endeavor to treat them in the way by which industrial health can best be served. Only secondarily are we interested in helping them as individuals. We believe our country's peril makes this our only proper attitude, and we are taking it seriously.

In closing, it is my belief that the interns and medical students of New England, in whose name the writer signed to dip his pen, are worthy of a higher expression of their interests and activities.

DWIGHT O'HARA, M.D.

FELTY'S SYNDROME

To the Editor The paper, 'Rheumatoid Arthritis associated with Splenomegaly and Leukopenia,' which appeared in the September 10 issue of the *Journal*, interested me particularly because the authors omitted a discussion of certain facts that may be of significance in explaining the etiology of this syndrome, originally described by Felty.

They failed to mention, for instance, that, in the cases reported by Hanrahan in 1932 and by Craven in 1934, the

patients experienced significant relief of symptoms and a rise in leukocytes to a normal level following splenectomy. In a third case, recently reported by Steinberg, the patient showed similar improvement.

Most disappointing was the fact that there was no attempt to correlate these cases with the newly recognized syndrome, primary splenic neutropenia, originally described by Wiseman in 1939. A detailed discussion of this disease has recently been given by Wiseman (Wiseman, B. K., and Doan, C. A. Primary splenic neutropenia; a newly recognized syndrome, closely related to congenital hemolytic icterus and essential thrombocytopenic purpura. *Ann. Int. Med.* 16:1097-1117, 1942). Seven such cases, exhibiting leukopenia, fever, hyperplasia of the bone marrow and splenomegaly, have been reported. In most of these, there was some arthritis.

The failure to establish infection as the primary cause of rheumatoid arthritis suggests the possibility of an error in metabolism as being an underlying factor. It is interesting to speculate the nature of this error. The occurrence of arthritis in people with primary splenic neutropenia and the improvement of the joint symptoms following splenectomy may offer a new concept of the pathogenesis of Felty's syndrome, as well as rheumatoid arthritis as a whole. If this type of arthritis occurs as a result of a chronic decrease in the number of circulating leukocytes, it is not unreasonable to suspect it may occur as a result of some pathologic alteration of the fundamental character of the leukocytes in the absence of leukopenia.

There is not enough evidence at present to assume that rheumatoid arthritis associated with splenomegaly and leukopenia and primary splenic neutropenia are the same or related syndromes. There is enough evidence, however, to warrant further study with this possibility in mind.

WILLARD H. WILLIS, M.D.

Slocum-Dickson Clinic
258 Genesee Street
Utica, New York

BOOK REVIEWS

A Primer on the Prevention of Deformity in Childhood. By Richard B. Raney, M.D., in collaboration with Alfred R. Shands, Jr., M.D. 8°, cloth, 188 pp., with 88 illustrations. Elyria, Ohio: National Society for Crippled Children, Incorporated, 1941. \$1.00 postpaid.

There has long been a need for a volume of this type. It describes in a clear, simple manner the usual deformities of the locomotor system, how they occur, and how they can be prevented. There are numerous drawings of deformities and of apparatus. It is shown that most skeletal deformities can be prevented, often by the use of simple measures. The book should be especially helpful to orthopedic nurses, physiotherapy technicians and social workers, as well as physicians, on whom rests the responsibility for the prevention of deformities.

Arthritis in Modern Practice: The diagnosis and management of rheumatic and allied conditions. By Otto Steinbrocker, M.D. With chapters on painful feet, posture and exercises, splints and supports, manipulative treatment, and operations and surgical procedures by John G. Kuhns, M.D. 8°, cloth, 606 pp., with 321 illustrations. Philadelphia: W. B. Saunders Company, 1941. \$8.00.

The authors have succeeded admirably in reducing to a reasonable compass the essentials of recent progress in

arthritis. The classification adopted is that commonly used in America, based on the belief that the proliferative type is the result of toxic influences, whereas the degenerative has no direct association with infections.

In the opinion of the reviewer, the chapters on fibrositis and on local and regional analgesic injection comprise the greatest contribution to knowledge of painful musculoskeletal disturbances. These, alone, make the book worth having. The inclusion of chapters on the technics employed in the management of arthritic sequelae adds to the usefulness of the book.

Our Sex Life: A guide and counsellor for everyone. By Fritz Kuhn, M.D. Second revised edition. 8°, cloth, 460 pp., with 41 illustrations. New York: Alfred A. Knopf, 1942. \$5.75.

This general treatise of twenty-three short chapters divided into seven hundred and thirty-five numbered sections is a translation of a German work. The book possesses some of the merits and demerits of recent German treatises for the sexual instruction of laymen: the colored illustrations are above average, and the range of topics is wide enough to take up most questions that trouble the average person; on the other hand, the book is not always accurate. There is a tendency to lean toward the bizarre in some of the case histories. Although better books are available for general instruction, this is a worthwhile addition to popular literature. Certainly, it is a great improvement over what was available a decade or two ago.

After giving a description of male and female structures and functions, the author discusses the hygiene of sex life, birth control, abortion, contraception, sterility, disturbances in sex life, such as impotence, frigidity and premature ejaculation, and the commoner diseases of sex life. Part VII is devoted to 'prostitution, and Part VIII to juvenile sex life; Part IX deals with the sex life of unmarried people.

Nutritional Deficiencies: Diagnosis and treatment. By John B. Youmans, M.S., M.D. Assisted by E. White Patton, M.D. 8°, cloth, 397 pp., with 16 illustrations. Philadelphia: J. B. Lippincott Company, 1941. \$5.00.

It is a paradox of modern civilization that, with the progress of society, concomitant problems have developed, one of the major ones involving the poor nutrition of the masses. The extreme poverty afflicting large numbers of men, women and children created medical as well as social difficulties. Vast clinical material, tantamount to mass experimentation, afforded opportunities for study that rapidly supplemented animal experimentation. Of the nutritional difficulties, vitamins play a major role.

The author has admirably sifted the data in a book characterized by an orderly and lucid presentation of the important aspects of deficiency diseases, with the greater emphasis on vitamins. Also included, however, are protein and mineral deficiencies.

Summaries, tables and laboratory procedures are other valuable features of the book. For one not in a position to undertake the laborious task of reviewing the massive literature, this volume will provide an adequate substitute.

The reviewer cannot refrain from echoing the sentiment that, after all, a normal diet in a normal person is an adequate diet. It is deplorable to contemplate the colossal sums of money expended in "over-the-counter" sales of vitamins to persons who are not the most in need.

(Notices on page x)

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THE SEQUELAE OF WAR HEAD INJURIES*

DANNY BROWN, M.B., D.Phil., F.R.C.P.†

BOSTON

EARLY in 1939, Air Commodore C. P. Symonds, consultant in neurology to the Royal Air Force and an authority on the subject of disability from head injuries, was planning the establishment of a central air-force hospital in England for neurologic problems from head injuries in flying personnel. He recognized the variety of special problems inherent in the assessment and adequate treatment of head injury in modern warfare, particularly the peculiar interrelation of surgical, neurologic, ophthalmologic and psychiatric problems involved. Colonel Hugh Cairns was, he found, already interested in neuro-surgical organization for the British Army, and it was proposed that the two plans be coalesced in a combined services hospital for head injuries. Arrangements were completed with the enthusiastic co-operation of the Directors General of the Army and Air Force medical services, but not until some months after the outbreak of war did the hospital begin to take shape. It was eventually opened in February, 1940, as an army hospital with some specially seconded Royal Air Force personnel. It received both Army and Royal Air Force casualties. I had the honor of being placed in charge of the Medical Division, which was entrusted with the original plan of Air Commodore Symonds, closely interrelated with the Surgical Division to which Colonel, now Brigadier General, Cairns was consultant. Air Commodore Symonds was not only the consultant to the Medical Division but also organized and supervised the Registry of Head Injuries, which is making a most valuable research correlation of all the data made available by this unique unit.

The following account is concerned with the assessment and treatment of prolonged sequelae of head injury, although other types of neurologic

disturbance also claimed attention. The surgical aspects of acute injuries have been commented on elsewhere.^{1,2} From the beginning, it was evident that, as had been foreseen, the proper treatment of the late effects of head injury under service conditions required a more than usually thorough preliminary examination. The large numbers of possible factors causing failure to return to duty following a reasonable convalescence from head injury (six weeks was the arbitrary time adopted) may be resolved into two chief categories—organic and psychoneurotic. It is essential to assess these factors accurately, for their treatment and disposal differ greatly.

The Registry has already collected complete data, including follow-up, on well over 1200 cases of head injury handled by the hospital. Complete analysis will ultimately be published by the British Medical Research Council, which finances this aspect of the work. The kind of problem involved can be estimated from my personal notes of the last 400 cases of persistent disability admitted by me for assessment. It must be emphasized that, although the hospital received acute head injuries from a large area and a majority of cases of persistent disability from all areas, these figures are highly selective, and complete data regarding all head injuries or all casualties cannot be published at present. I purposely omit the patients with recent injuries who made rapid recoveries. Out of the 400 cases of unduly delayed convalescence, 38 patients had suffered gunshot wounds of the head, 13 injuries to the head in aircraft crashes, 303 head injuries from other trauma (motor-cycle or other accidents with vehicles, tanks and so forth), and 46 from recurrence of symptoms from old head injury dating from before the war. Of these 400 men, 22 (5.5 per cent) were suffering from *traumatic epilepsy*, 116 (29.0 per cent) from other *organic defects*, and 262 (65.5 per cent) solely or chiefly from *psychoneurosis*. In the group of 38 gunshot wounds, 3 pa-

*Presented in abbreviated form at the annual meeting of the Massachusetts Medical Society, Boston, May 27, 1942.

†Professor of neurology, Harvard Medical School, director of the Neurological Unit, Boston City Hospital, and Captain, Royal Army Medical Corps Reserve.

tients suffered from epilepsy, 19 were still disabled by organic (structural) disorders, and 16 by psychoneurosis. Of these, 21 were subsequently fit to return to duty, and 17 were discharged unfit. The proportion of the 400 returned to duty was almost exactly the same.*

It is clear that disorders such as hemiplegia and aphasia following a laceration of the brain are the result of damage to structure; on the other hand, a prolonged disability, such as insomnia, tremors, depression and fear of crowds, following a trivial head injury in a person who was previously prone to such symptoms is palpably psychoneurotic. The actual decision is, however, seldom so clear cut, and with increasing experience of all classes of injury from a variety of circumstances, more and more involved mixtures of organic and functional sequelae were defined by modern methods. Thus, to quote extremes, the aircraft pilot who has made a perfect recovery from a surgical head wound, has shown himself fit for every form of strenuous physical exertion, and pesters everyone to be allowed back to duty may develop a serious flying error on return to his squadron owing to a previously undisclosed nervous anxiety caused by the terrifying circumstances of his accident. Apart from the danger of further accident, the subsequent treatment for this neurosis involves a waste of time that is saved if the liability is diagnosed earlier. The patient who has suffered an apparently trivial head injury and later wanders, with loss of memory, is sometimes shown by the electroencephalogram or subsequent attacks to be suffering from epilepsy, although his original wandering fugue was hysterical and his memory is recoverable under Amytal. The patient behaving in a clearly neurotic manner may be found to have a xanthochromic spinal fluid, and the real reason for the failure to return to efficient duty of a patient with optic atrophy in one eye may be related not to his vision but to his anxieties about his relatives at home. An unsuspected abscess may be discovered by a chance air encephalogram, and an unsuspected but fundamentally important emotional factor may slip out in a casual remark.

Moreover, in the modern soldier, the tremendous tension of modern warfare — the noise, the rush of movement, the variations in climate and, above all, the heightening of individual responsibility — renders accurate assessment of great value in the decision regarding the return to duty and the kind of duty; such a decision is even more important in the airman, and may present the utmost difficulty in officers and commanders. When downgrading of responsibility appears desirable

on medical grounds, or when the question of invaliding out of the service arises, further psychologic considerations complicate the picture and must be carefully weighed regarding individual personality if successful adjustments are to be achieved.

The medical services of the United States are no doubt fully alive to and prepared for the inevitable problems that will arise in these respects, but discussion of them, in the light of over eighteen months' experience of this kind of work before I was transferred to my present assignment, may be of interest.

GENERAL CONSIDERATIONS

Traumatic Epilepsy

The incidence of traumatic epilepsy following head injury will no doubt be a surprise to some, especially in view of the low figures of Sargent³ after World War I (4.5 per cent in 18,000 cases) and of Stevenson⁴ (1.5 per cent in 17,300 cases). But in the present whole series, the incidence was even higher than in the 400 cases mentioned above, for the Registry had filed 53 cases (16 focal and 37 generalized) out of a larger group of 630 fully documented consecutive patients. Of these, 22 had had attacks within one month, 16 in one to six months, 8 in six to twelve months, and 5 in two to five years. Of the 22 having convulsions within one month, only 6 had suffered gunshot wounds.

Traumatic epilepsy is a complication of localized destruction and scarring of cerebral tissue, particularly from so-called "open injuries," when the dura has been penetrated. The attacks had rarely remained sufficiently localized to give good results from excision of the scar (1 case in 400 head injuries, and this was a closed head injury). Closed head injury undoubtedly can give rise to traumatic epilepsy, as Symonds⁵ has remarked; but the liability to epilepsy is not proportional to the severity of injury, even with prolonged unconsciousness and resulting intellectual defect. Of 87 patients with post-traumatic amnesia longer than seven days, only 3 suffered from epilepsy (2 generalized, 1 focal). One of these had shown evidence of focal brain injury, and it is likely that this was present in the other 2. Traumatic epilepsy is therefore not the result of a generalized damage to the brain. These figures are in accordance with those of Ascroft,⁶ who analyzed material from World War I after an interval of seven to twenty years; in his series, the incidence of epilepsy was 34 per cent and, in cases in which the dura had been penetrated, 45 per cent. In other series, Wagstaffe⁷ found a general incidence of epilepsy in 10 per cent of 377 cases, Rawling⁸ in 25 per cent of 425 cases, and Credner⁹ in 38.2 per cent in 1990 cases after five years. Cred-

*Symonds has published in the July, 1942, issue of the *Proceedings of the Royal Society of Medicine* the results of a follow-up of 871 cases, including the 400 mentioned here, that show 68 per cent successful return to service duties.

ner noted that 81.1 per cent of cases with dural penetration develop epilepsy. The variability of these figures depends on the manner of selection of the head-injury series, and the length of time under observation. The Registry will afford more accurate statistics as time passes. It must be borne in mind that the material discussed here includes few mild head injuries (concussion with full recovery within six weeks) and not many of the severer injuries, and consists of selected problem cases of intermediate type.

This situation is serious, and few surgeons appreciate the disabling possibilities of the simplest dural wounds. The problem is even more complicated in the common type of modern bomb or splinter injury, in which small fragments of metal and bone scatter widely through the brain, and lodge in the most inaccessible places. Such foreign bodies appear to cause no trouble, for they are seldom infected, and after débridement of the most superficial, the others may remain until more is known about their epileptogenic properties. So far as present hypothesis goes (Penfield¹⁰), it is the cerebrodural scar that is epileptogenic, not necessarily the foreign-body reaction, and experience with these very small splinters of bomb casings certainly bears this out.

The finding of Wagstaffe,⁷ Symonds⁵ and Ascroft⁶—that epilepsy occurring within the first four weeks after injury has an excellent prognosis—was fully borne out in our cases. The electroencephalogram shows widespread activity of epileptic type in many cases of laceration of the brain without clinical evidence of convulsions (Williams¹¹), and this also rapidly subsides without aftereffect. There is, however, an exceptional and rare type of case in which a relatively trivial injury has been followed by persistent severe fits of a generalized kind, with an electrical record in the intervals between the attacks resembling that of deteriorated idiopathic epileptics. A previous constitutional liability to epilepsy is then to be suspected, and the prognosis is poor.

Other Organic Disabilities

Of the other consequences of structural damage to the brain, hemiplegia, paraplegia from wounds to the vertex, hemianopia or scotomatous field defects and dysphasic-dyspraxic disorders are obviously serious disabilities. Much can be done to rehabilitate such men for some form of civilian employment, with training in special skills. The same training facilitates the speed of recovery of lesser disorders of motor function, sensation, speech and vision. Persons who are really effective in designing exercises in muscle re-education, or to obtain sensory co-ordination, and who can direct

speech therapy and visual exercises are few. Moreover, such treatments are time consuming. The experienced physician therefore early selects cases with a good prognosis for return to duty and retains them in the service hospital, advising early discharge of the remainder to civilian rehabilitation centers. The general nature of the problem is well described by Goldstein¹² in a monograph in which he summarizes his experience in World War I. He gives an excellent description of methods again found useful both in accurate assessment and in rehabilitation. It is not practicable to rehabilitate all men in a service hospital that has a large waiting list.

In cases requiring bony repair, with fractures into a frontal sinus,¹³ with retained foreign bodies, and with jaw, facial, ophthalmic and other injuries, surgical consultations and conferences regarding the main disability are indicated; if necessary, the patient is transferred to a surgical division, to return later for the neurologist's supervision during final convalescence. In some cases of recent injury (and usually in hitherto unsuspected scalp wounds), a subdural hematoma, an abscess or necrosis of the bone requires direct surgical relief.

POST-TRAUMATIC GENERAL CEREBRAL SYNDROME

Prominent in the sequelae of head injury are headache, usually associated with vertigo, difficulty in concentration and insomnia, with or without depression. This whole group, variously described as the "postconcussion syndrome," "post-traumatic general cerebral syndrome" (Foerster¹⁴) and "minor contusion syndrome" (Symonds¹⁵) is by far the commonest symptom complex that develops out of craniocerebral injuries. It follows all kinds and degrees of head injury, although many writers have commented on its absence in many cases of severe laceration of the brain (Russell,¹⁶ Schaller,¹⁷ Strauss and Savitsky¹⁸ and others). A general discussion of the symptoms is given by Symonds.¹⁵ Schaller¹⁷ subdivides cerebral post-traumatic disorders into the "post-traumatic psychoneurotic state," with symptoms of headache, dizziness and hysteria, and the "post-traumatic concussion state (encephalopathy)," with loss of concentration, defective memory and vertigo. This presupposes that headache, dizziness and so forth are psychoneurotic symptoms, and some frankly ascribe the combination to a compensation motive. Others^{16, 19} have pointed to its occurrence in cases without compensation factor of any kind. The subject has been very adequately reviewed by Strauss and Savitsky.¹⁸ Penfield and Norcross²⁰ claim that post-traumatic headache is due to meningeal adhesions demonstrable by their special

technic for showing subdural air, and that "the patient's description of his symptoms makes the diagnosis certain and allows the understanding physician to recognize the true sufferer." They do not specify the elements in the description on which this sanguine statement is based. It is probable that headaches of organic and psychoneurotic types should have different clinical characteristics. With my associates, I attempted, unsuccessfully, to define such differences as may exist. We found that clearly demonstrable meningeal scarring was occasionally the site of localized ache, but usually not. Subdural air has been seen in encephalograms without previous injury (Lemere and Barnacle²¹) and is not regarded as of value in diagnosis. On the other hand, the depressed psychoneurotic patient frequently complains of a steady, dull discomfort over the whole head, unaffected by posture or external events, except excitement. This type of headache is well recognized as of psychoneurotic origin. But this was not the answer. The common paroxysmal generalized or one-sided headache—diffuse but usually frontotemporal, affected by posture as well as exercise or excitement, rising to intensities of sharp pain followed by numbness, and associated with swimminess on or after stooping, with loss of concentration and, usually, periodic insomnia—was as commonly associated with frank psychoneurosis as with severe brain injury. One difference, however, that probably accounts for the denial of many that such a post-traumatic syndrome is associated with severe head injury, is its delayed onset in these cases, so that at the time of discharge from the hospital or the completion of usual convalescence, the syndrome has not yet appeared.

Among other names, the group of symptoms is commonly called the "post-concussion syndrome." If by concussion is understood immediate loss of consciousness due to injury of the head, associated with loss of memory for this time, and retrospective loss of memory of the injury and the events immediately preceding it, it is certain that the post-traumatic general cerebral syndrome can occur without concussion.

Something must be said of the pathology of concussion. Experimental evidence has shown that concussion is not associated with any cerebral lesion recognizable by the naked eye, or by the microscope with any staining process at present available.²² It is not due to any effect on cerebral blood vessels, although changes in circulation accompany its later stages. It has a characteristic effect on the cerebral electrical record,²³ and is a phenomenon common to any nervous center subjected to sufficiently sudden physical stress. It

is a transient paralysis of nervous function. In head injury, it is generalized, and is produced by sufficiently sudden acceleration or deceleration of the head. It is thus often absent in crushing injuries, even though they cause multiple fractures and other damage,²² for the head may not be subjected to change in velocity.

It is common knowledge that extradural hemorrhage, subdural hemorrhage or cerebral contusion can be produced by an injury that does not concuss the patient. These effects are due to local tears or distortions. Clinical evidence shows that medullary contusion, with or without subarachnoid hemorrhage, can be produced without concussion.²⁴ In war surgery, the absence of concussion in penetrating injuries of the brain has been commonly noted (Léri,²⁵ Denny-Brown,²⁴ Denny-Brown and Russell²² and Eden and Turner²⁶). Concussion is the outcome of *general commotion* of the brain, which is slighter or absent when penetration occurs, especially with small fragments.

Recently, fat embolism has been held responsible for concussion (de Gutiérrez-Mahoney²⁷). This, however, did not occur in my experimental work on concussion.^{22, 23} Furthermore, the recognized clinical disorder due to fat embolism is delayed in onset and characterized by unmistakable features in pathology (Osnato and Giliberti²⁸ and Robb-Smith et al.²⁹). In all the cases of acute head injury in this series, there was only 1 patient who clearly suffered from fat embolism—that is, fever, petechiae and fat in the urine. The patchy damage it causes in the cerebral cortex is identical with the patchy cell changes in the cerebral cortex found months or years after injury that are described by Winkelman and Eckel³⁰ and that are considered by them to be the basis of the post-traumatic general cerebral syndrome.

The common types of severe head injury show various combinations of a series of separate clinical entities, including medullary contusion, subarachnoid hemorrhage, general cerebral concussion, cerebral contusion, laceration, intracerebral and extracerebral hemorrhage, subdural collections of blood or fluid, skull fracture and, sometimes, fat embolism. Each or all may be followed by the syndrome in question. Despite the influence of posture, one should regard the syndrome at this stage as a *particular mode of reaction to head injury*, without specific identification with either an organic or a functional basis. In this sense, it is directly comparable to the "effort syndrome," recognized by Wood³¹ and others as related to either cardiac disease or cardiac neurosis and, in both, a type of reaction to cardiac symptoms. Only in this way does it appear possible

to reconcile the appearance of the post traumatic syndrome in association with a great variety of types of injury. Some illustrative examples indicate the general nature of the problem.

CASE 1 Driver R. L. B., aged 21, was thrown from an army car on January 10, 1940. There was a retrograde amnesia for a few seconds and a blank in memory for 10 minutes after the injury. The patient then vomited and was taken to a hospital. There was a bruise in the right temporal region, but no other injury. Right sided headache continued for 3 days and then ceased. The patient

had nightmares of falling and of being wounded. He was sure that he had fractured his skull and damaged his brain.

He responded immediately to psychotherapy but relapsed, with further headache and complaint of dizziness at the prospect of return to duty, and was eventually discharged as permanently unfit.

This patient presented the post traumatic syndrome in characteristic form, with typical postural reaction to the headache and even syncopal attacks, yet the vasomotor instability had antedated

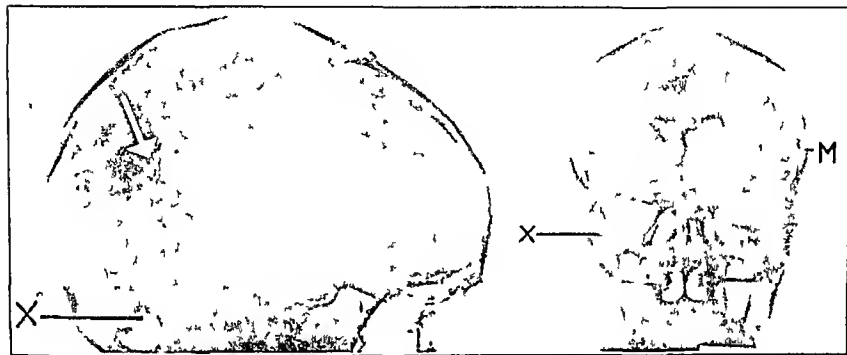


FIGURE 1 Case 2

In the lateral view of the skull just below the arrow is a small puncture of entry of the bomb fragment with underlying gray flakes of bone and small metal particles. The main metal fragment had crossed the cavity of the skull to lie on the tentorium where it is seen through the mastoid cells (to the right of the line x). The anteroposterior view with the ventricles filled with air shows enlargement of the ventricle on the side of entry in the metal fragments (m and x).

felt well and was discharged to duty after 3 weeks. In May, after 10 days of continuous fighting, he became very exhausted and once fainted for a few minutes. He came through Dunkirk without incident but a month later began to suffer from generalized headache every 3 or 4 days lasting all day, more pronounced with exertion or excitement and associated with dizziness on movement. In the next month, he fainted four times, usually after some physical exertion. His mother and a cousin had suffered from psychoneurosis, and his mother had fainted on several occasions. He had been an average scholar, had no ways being a worrying sensitive fellow, and had once fainted at a camp at the age of 12 years.

He was of pale complexion and poor physique, but had no sign of injury to the head and no abnormal physical signs. X-ray films of the skull showed no bony injury. An electroencephalogram was normal. The red-cell count was 4,175,000 with a hemoglobin of 85 per cent. After prolonged interviews the patient recollected being terrified of traffic after his accident and had vivid recollections of it for some weeks. He explained how he then became less nervous, but after Dunkirk had vivid recollections of the fighting and became terrified of the possibility of pain or the sight of blood. He said, "I could not go through that again." He developed fears of traffic or air raids, and

the relatively slight injury, and the whole syndrome was considered to be a result of constitutional psychoneurosis.

CASE 2 Corporal Y., aged 22 years, sustained small cuts in the scalp from fragments of a bomb in May, 1940, and was concussed for 5 minutes. The scalp wounds healed rapidly, and he did not complain of any further disorder. In August, during another bombing, which did not harm him, he developed headaches on exertion, dizziness on bending, emotional lability and insomnia. These symptoms increased in intensity, and after 4 months of disability from them, examination revealed an excessively nervous man without sign of damage to the skull or nervous system. He admitted tremor during the second bombing and that he had at that time deserted his post to take cover, even though he had not been discovered. He confessed inability to face further service and further disclosed a matrimonial tangle of considerable proportions. X-ray films disclosed unexpectedly, several bomb fragments in the brain (Fig. 1) and a small parietal portal of entry only a few millimeters in diameter. The patient failed to make adequate response to psychotherapy, and since there was a family history of severe nervous breakdown, he was discharged.

In this case, in spite of the presence of foreign bodies, the post-traumatic syndrome was considered to be purely psychoneurotic.

The following case is an example of local cerebral contusion without concussion.

CASE 3. Guardsman A. C., aged 23, was injured on May 15, 1940, defending a canal bank at Louvain. He was struck tangentially by a bullet, which tore a 7.5-cm. hole in his steel helmet and made a cut 3.5 cm. long in the midoccipital scalp, 5 cm. above the occiput. He did not lose consciousness, and fired three more shots, but could not see plainly—"like through a mist." He crawled back to a trench and walked a mile to his medical officer. In this time, his vision was becoming dimmer, and when he arrived at his dressing station he could not distinguish light from dark. The wound bled severely and after morphine the patient remembered no more until 2 hours later, when he awakened in a casualty clearing station with severe headache but could see a little better. For

times, a cough caused a sharp stab but no lasting pain. Bending made the pain worse; later, the patient was more comfortable when lying down. In the 4th week, he could read small print, but the effort precipitated headache. In the 6th week, reading no longer caused headache, and his distant vision was clear for the first time. Headache on exertion became very infrequent, although of the same type and lasting for some hours. By the 9th week, the



FIGURE 2. Case 4.

The lateral view of the skull shows metal and bone fragments. The portal of entry is very small and partly obscured by the lowest metal fragment. The ventricles were partially filled with air, and the patient was lying occiput down, so that there is a fluid level. The anteroposterior view shows distortion of the ventricle toward the fragments. All disability was nevertheless relieved.

the next few days, intermittent, severe frontal headache, radiating to the nose, lasted for hours and continued for the next 3 weeks, at first daily, with three bouts in the last week. Vision slowly improved, at first for near objects, with a shimmering mist blurring anything farther away than his own hand. No hallucinations occurred. The headaches usually appeared in the afternoons, and were immediately made worse by any movement. At other

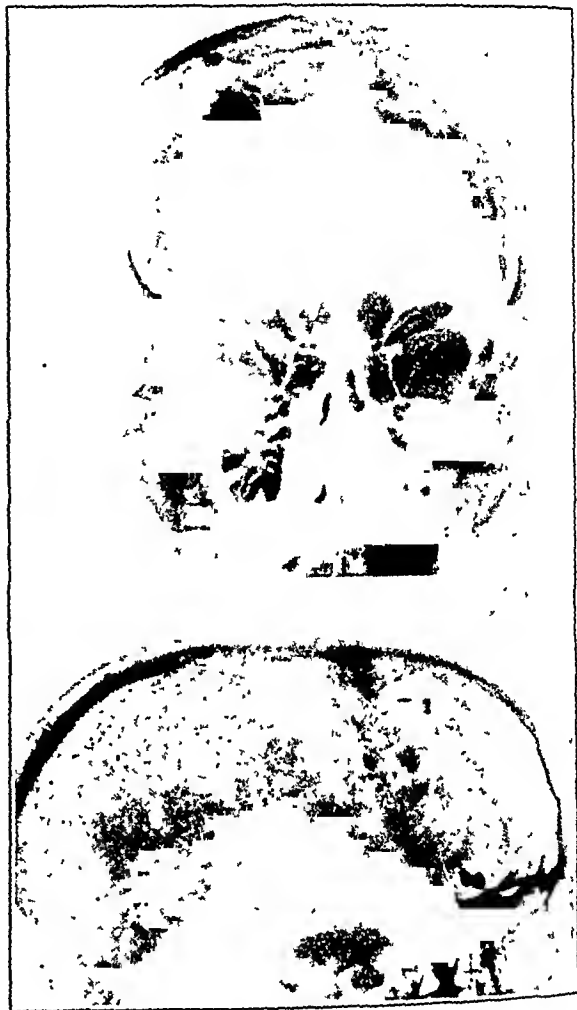


FIGURE 3. Private W.

These are lateral and posteroanterior views of the skull of a patient who was not concussed by the penetrating bomb fragment, which crossed the frontal lobes to lodge above the opposite orbit. Flakes of bone lie directly beneath the point of penetration. After débridement, including removal of the bone flakes but not the metal fragment, he made an excellent recovery, without epilepsy or other disability.

patient had ceased to have headache except after very severe exertion or excitement, and felt well in all other respects. There had been no faints, and he had slept well all through. His vision was 20/30 in each eye, there was no field defect, the wound had satisfactorily healed, and x-ray films showed no bony damage. After a graduated convalescence, he returned to duty and remained well for at least a year.

This patient evidently suffered a contusion of the occipital lobes, but was not concussed. The local

brain injury conditioned a post-traumatic headache, but at no time was there any symptom that could be construed as being emotional or psychoneurotic. The subsidence of the headache paralleled

local brain injury. They were cited to show that contusion, concussion, foreign bodies and even scarring of the brain substance are not necessarily factors in inducing continued headache. Further-

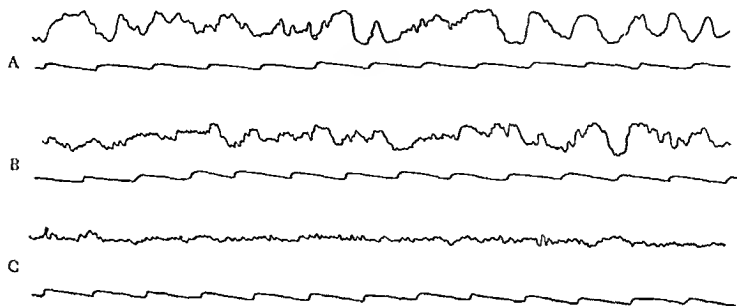


FIGURE 4 Case 3

These electroencephalograms were made from bipolar parietal leads on the left side A, seven days after the injury, B, three weeks after the injury, and C, ten weeks after the injury. The time tracings show 1 second notches. The disturbance was identical in all other leads on both sides at each stage.

leaded the disappearance of the contusion as judged by the disappearance of the visual symptoms.

A similar history, with concussion and brain injury and spontaneous recovery follows.

CASE 4 Private R. W. D., aged 21, was injured in Flanders on May 22, 1940. He remembered the whistling of a bomb and that he threw himself on the ground; he remembered vaguely an explosion and biting sensation and then nothing until he was being bandaged with a field dressing less than 5 minutes later. His steel helmet had been blown off by the bomb explosion, and he had a scalp wound, he had difficulty in expressing himself although he was well aware of his surroundings. He had headaches but no giddiness for the next 2 weeks. After 2 weeks, he could speak a few words, and gradually his speech returned completely in the next 2 months. He had at no time any difficulty in understanding written or spoken speech or in writing what he wished to say. After 3 months, he complained only of headache after severe exertion. Examination at this time revealed a slight right facial weakness, and a stellate scar in the left frontoparietal region, but no other abnormality. Speech was occasionally hesitant. X-ray films showed a small opening in the left parietal bone, with small fragments of bone and bomb splinters in the brain and with some enlargement of the ventricle by the resultant scar, as shown by air encephalograms (Fig. 2). Electroencephalograms showed a persistent low voltage wave focus just posterior to the wound of entry. No further surgical treatment was advised, and with graduated exercise the patient was entirely free from headache by October, returning to duty in November. He had remained well when last heard from, approximately 6 months later.

The patients in Cases 3 and 4 had excellent personal and family histories, and this no doubt contributed to their complete recoveries, despite severe

more, 'organic' headache is not necessarily associated with postural giddiness. There were a number of other similar cases of gunshot penetration with complete recovery. In one such patient, a fragment traversed both frontal lobes (Fig. 3).

Three cases of transverse through and-through bullet wounds of the frontal lobes showed severe intellectual impairment but no evidence of post-traumatic syndrome. Other cases, with severe paralysis, also failed to develop the syndrome, but possibly because the disability prevented exertion, which is one of the provocative factors.

Another type of case, however, is more frequently associated with persistent post-traumatic syndrome, and in its severest form is usually called "traumatic delirium" or "traumatic stupor,"³² according to whether or not restlessness is prominent.

CASE 5 Sergeant R., aged 24, sustained a bilateral wrist fracture and a scalp bruise on the right temple in a motor cycle injury on November 14, 1940. He was admitted in coma,* with bleeding from the right ear. The pupils were small and equal, the tendon jerks brisk, and the plantar responses flexor. The pulse was 128 to 132, and the blood pressure 135/90. After 24 hours, the patient responded to questions by inarticulate noises, and resented interference, there was photophobia, and the plantar responses became extensor. After 4 days, he began to make intelligible remarks, such as 'What's that?' 'Don't do that' and 'Is Mother there?' He was deeply confused,

*The Committee on Brain Injuries of the British Medical Research Council has compiled a standard definition of coma commonly used in head injury.³² Of a patient in coma is preferred to unconscious and defined in terms of reaction to stimuli.

and the next day, in response to the question about how he felt, said: "Not too bad, doctor. I go to the hospital every morning." His restlessness increased, especially at night, and he shouted if interfered with. He was doubly incontinent. After 14 days, he could mumble his name and address in response to questioning, and occasionally showed his teeth or followed a finger with his eyes, if requested. The plantar responses returned to normal, and the incontinence lessened and disappeared. The patient remained grossly disoriented in time and place, and had



FIGURE 5. Case 5.

These lateral and anteroposterior views (occiput down) of the skull, after air encephalography, show general dilatation of the ventricular system.

no memory of the day before, or even what meals he had had that day. X-ray examination of the skull was entirely negative. The cerebrospinal-fluid pressure was 170 mm., and the protein was 35 mg. per 100 cc; no cells were present.

Gradually, co operation and orientation returned, passing through a stage of confabulation, with some perseveration in speech and ideas but no dysphasia. The memory was severely affected, and the patient often relived events of years or months before. Christmas Day, in the 6th week of his illness, was the first current event to remain in his memory and also subsequently marked the end of post-traumatic amnesia. The retrograde amnesia, at first of 3 months with "islands," gradually narrowed down to an irreducible minimum of a week.

The patient steadily improved, but with persistent slowness and difficulty in concentration. His memory remained

grossly defective (except for retaining serial digits, but he had been an accountant). He was emotionally labile and disturbed by his difficulty in concentration.

Not until he began to get up each day did he complain of headache, generalized, increased by movement, concentration, noise or cough and lasting for some hours on his return to bed. He felt giddy if he turned quickly, and occasionally faint. When, after some weeks, he was given graduated exercise, he reacted by a "catastrophic reaction," failing suddenly on every test at an easy stage, and became depressed and introspective. Only with return to lesser grades and with great patience was he induced to further graduated activity. When well enough to care for himself, he was discharged for further rehabilitation in a civil hospital.

Throughout his illness, this man showed gross electroencephalographic abnormality. Large slow waves at the rate of 1 per second were present throughout the two hemispheres for the first fortnight (Fig. 4), and then gradually lessened with the appearance of faster rhythms. After 3 months, the base line still showed traces of the slow waves. There was not at any time a focus of abnormality.

This patient never showed any evidence of damage to a localized part of the brain. There was no evidence of fat embolism, although the urine was not examined for fat. The cerebral disorder was generalized and severe, and was followed by persistent intellectual deficit. It is an open question whether the emotional disorder and the post-traumatic syndrome were directly induced by the injury or were a psychoneurotic reaction to the patient's awareness of his mental limitation. The family and past histories were irreproachable; he had been a successful businessman before enlistment. An air encephalogram after 3 months showed generalized dilatation of both lateral ventricles, indicating generalized cerebral atrophy of mild degree (Fig. 5). In view of the persistent electroencephalographic abnormalities, which after 3 months took the form of small runs of slow waves at times (possibly indicating some tendency to epileptiform manifestation), the whole disturbance was regarded as directly consequent on the traumatic damage to the brain, and visualized as an extreme example of concussion.

Slighter varieties of this type of disorder, which might be called traumatic coma followed by confusion, are not uncommon. All degrees are met, down to such brief events as are more usually termed concussion, with correspondingly lesser degrees of, or absence of, residual intellectual impairment. An intermediate degree is illustrated by the following case.

CASE 6. Gunner J. B., after a motorcycle accident, was deeply comatose for 24 hours, and confused and restless for 21 days, with normal cerebrospinal-fluid pressure and contents. The electroencephalogram showed large slow generalized waves all this time. After a slow convalescence,—3 months,—the patient was able to saw logs without symptoms. The electroencephalogram was not quite normal, and all memory and other intelligence tests gave a poor response (for example, the patient retained only six digits). On return to duty after 4 months, never having had a headache, he immediately broke down, became very emotional, complained of severe headache on any exertion and of giddiness on bending or turning suddenly or on looking up or down, insisted that he was

anxious to return to duty, and rapidly responded to psychotherapy. At the urgent request of his commanding officer, he was allowed to return to duty after further convalescence, subsequently relapsed and was eventually

to one or both of two factors. unduly prolonged coma and confusion following the injury, indicating concomitant severe generalized disturb

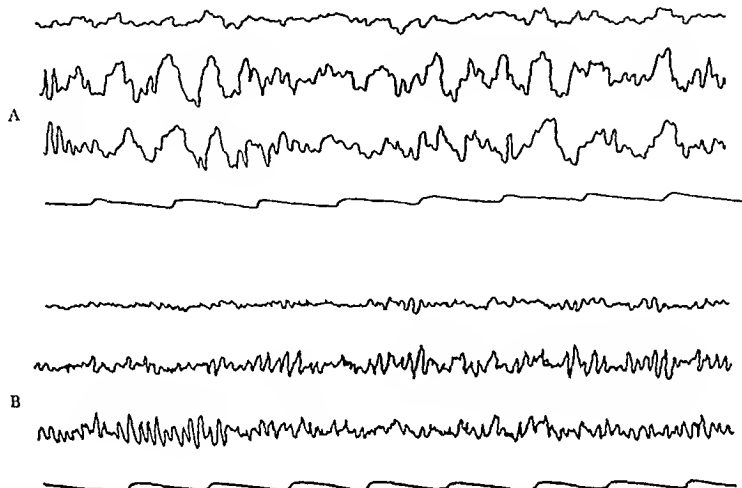


FIGURE 6 Case 6

Each of these two sets of electroencephalograms was made from frontal parietal and occipital leads, placed from above downward A, twenty days after the injury and B, five months after the injury. The time intervals are one second apart. In B, traces of 2 second and 3 second waves are still seen.

invalided permanently unfit (This case has been reported fully, with electroencephalographic records, by Williams¹¹). The electroencephalogram still showed traces of slow waves at 3 to 8 per second after 5 months (Fig. 6).

The ultimate breakdown in this case was clearly psychoneurotic and was conditioned by anxiety about the future. Nevertheless, it must be admitted that a certain degree of impairment of judgment could still be demonstrated by careful tests, that the patient always had been a poor scholar, although his family and personal histories were otherwise good, and that such intellectual impairment as directly resulted from the injury may in fact have been the only cause of the failure to reattain an already limited adaptation to army life.

One may contrast patients who suffered comparable direct cerebral gunshot injuries, both perhaps with some slight residual disability, and whereas one made an excellent recovery, the other was held back by general post traumatic symptoms. The failure of the second was regularly traceable

ance; and a history of liability to psychoneurosis or failure in adaptation in the personality or family history. In this group also fall the morons and chronic psychopaths whose capacity for adaptation is already limited.

(To be concluded)

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ACUTE PERFORATION OF ULCERS OF THE STOMACH AND DUODENUM

CAPTAIN HOWARD ULFELDER, M.C., A.U.S.,* AND ARTHUR W. ALLEN, M.D.†

RICHARDSON¹ reviewed the subject of acute perforation of ulcers of the stomach and duodenum from the data available at the Massachusetts General Hospital up to 1916. It is our purpose to present a study of the records of such patients from that date up to and including the year 1940. Richardson reported 103 cases with a mortality rate of 44.2 per cent. At the time of his writing, it was evident that the diagnosis was rarely difficult and that the best immediate results were obtained by simple closure of the perforation. There was at this time, however, a definite predilection for concomitant gastrojejunostomy in the good-risk patient. Moreover, the methods used for removing the extravasated fluid from the abdomen were variable. These technical differences persisted to some extent through the next decade. The last three five-year periods under discussion in our presentation, however, are comparable on the basis of the technic used, and were almost completed by the time the use of the sulfonamides had become common practice.

In the twenty-five-year period from 1916 to 1940, there were 334 admissions to our clinic with acute perforation of an ulcer of the stomach or duodenum. The diagnosis in all but 4 of these cases was confirmed at operation or autopsy. In one of the 4 exceptions the patient entered the hospital moribund, with a history and physical examination consistent with long-standing ulcer and acute perforation of thirty-four hours' duration. Operation was not performed and autopsy was unobtainable.

The other 3 patients survived without operation, and all the cases fulfilled the following criteria: history compatible with recent perforation; physical signs on admission consistent with peritonitis, free air under the diaphragm demonstrable by roentgenogram; and ulcer shown by a subsequent barium meal.

Only 13 patients, or less than 4 per cent of the entire group, were women. This ratio of 1:25 is interesting, since the sex ratio of ulcer in general is approximately 1:6. In fact, the proportion of women with ulcer who meet with the complication of perforation is somewhat in accordance with the peculiar protection they seem to possess from fatal hemorrhage from ulcer.² The incidence of the other chief surgical complication of ulcer—namely, cicatricial obstruction—is more nearly equal in men and women. It has been suggested that gastric ulceration in women is more apt to be benign than it is in men. Although our figures are not large enough to assure us of this fact, we are inclined to believe that it is not true, but that the same suspicion regarding malignancy should be held in both sexes.³ Six of the female cases of perforation were duodenal and 6 were gastric; 1 patient recovered without operation. Although there were 5 deaths in these 13 cases, the group is so small that we can only surmise that acute perforation of ulcer in women, although much rarer than it is in men, may, when it occurs, be more hazardous.

Considering only the 321 male cases in our series, we can divide them according to location of the ulcer as shown in Table 1. This would seem to indicate that the risk from perforation of an

*Assistant in surgery, Massachusetts General Hospital (on leave of absence)

†Chief East Surgical Service, Massachusetts General Hospital; lecturer on surgery, Harvard Medical School

ulcer proximal to the pylorus is slightly greater than if it occurs in the duodenum. Although these figures must encompass a definite slight error, owing to the operator's inability to determine invariably the exact location of the ulcer, the ratio of

TABLE 1. *Incidence and Mortality according to Location (321 Cases).*

LOCATION	NO. OF CASES	NO. OF DEATHS	MORTALITY %
Duodenum	218	59	27.1
Stomach	70	21	30.0
Jejunum	1	0	0.0
Unspecified	32	3	9.4

gastric to duodenal in this group is nevertheless comparable to that found in our clinic for other complications of ulcer.⁴

Nine patients in the entire group had already survived a previous perforation. Strangely enough, all these recovered from the second episode. It is unlikely that this was merely coincidence; more probably the patient, recognizing a recurrence of his former symptoms, delayed less in obtaining treatment. Doubtless he called attention to his previous condition and made it easier for his physicians to make the diagnosis; thus the all-important time factor was utilized to his advantage.

Often the question arises regarding the proper treatment for the patient who has recovered from acute perforation. How persistently should palliative management be carried out after perforation? Should such a patient be subjected to a radical operation if symptoms persist or if conditions are such that proper self-care is unlikely? The danger of a second perforation has often been raised. It is, of course, impossible to make any blanket rule covering the situation; we do believe, however, that patients recovering from perforation should be carefully followed and the same principles of good ulcer management carried out as in those who have not suffered this complication. If the response to conservative treatment is satisfactory, there is no reason to classify them in a separate category. In fact, such patients are probably no more likely to be invalidated by their malady than is the average ulcer patient. If the complication of cicatricial stenosis, massive hemorrhage or intractability does occur, then surgery is justifiable.⁵

There was 1 case in which simultaneous perforation of more than one ulcer apparently occurred. This was unrecognized at operation, and the patient succumbed to peritonitis. Such a possibility is unlikely, and it may reasonably be suspected that the second ulcer perforated during the convalescence following the suture of the first.

Certainly there is no way to foresee such a complication, and this incident does not warrant extensive exploration to avoid overlooking a double perforation. The dangers of too much handling of tissues, under these circumstances, far outweigh the risk of overlooking a second perforation.

If our series is divided into its component five-year periods, as shown in Table 2, it is apparent that as early as 1920 the results of treatment became stabilized. It is also obvious, in spite of the elimination of drainage, concomitant gastroenterostomy and so forth, as well as the marked improvement in anesthesia, fluid balance, blood chemistry and other preoperative and postoperative adjuvants, that there has been a striking failure in lowering the mortality rate. Since an increasing

TABLE 2. *Incidence and Mortality according to Five-Year Periods (334 Cases).*

PERIOD	NO. OF CASES	NO. OF DEATHS	MORTALITY %
1916-1920	36	11	30.6
1921-1925	43	11	25.6
1926-1930	90	24	26.7
1931-1935	74	20	26.5
1936-1940	91	24	26.4

number of perforated ulcer patients have been treated in our clinic in the last three five-year periods, with a variation in mortality of less than 0.5 per cent, we have further analyzed this group of 255 patients to see whether any light can be thrown on the problem.

In Table 3, we have regrouped these cases according to the season of the year in which they occurred. Thus, it appears that during the winter

TABLE 3. *Incidence and Mortality according to Seasons (255 Cases).*

SEASON	NO. OF CASES	NO. OF DEATHS	MORTALITY %
Winter	59	22	37.3
Spring	64	17	26.8
Summer	56	13	23.2
Autumn	76	16	21.0

months the mortality is highest, while during the autumn it is definitely at its lowest point. In an effort to account for this variation, we have plotted in Figure 1 the curves of yearly death rates from acute respiratory-tract infection in Massachusetts and of the mortality rates from perforated peptic ulcer in our clinic. Although these curves are scarcely comparable, it is obvious that they tend to parallel each other, particularly in that no peak in the former curve is without its counterpart in the latter. The sharp drop in both curves in 1940 is doubtless due to the universal use of

sulfonamides. It appears, therefore, that there is some relation between the mortality rate for perforated ulcer in our clinic and the virulence of the current respiratory-tract infection in the community. In support of this hypothesis are the ob-

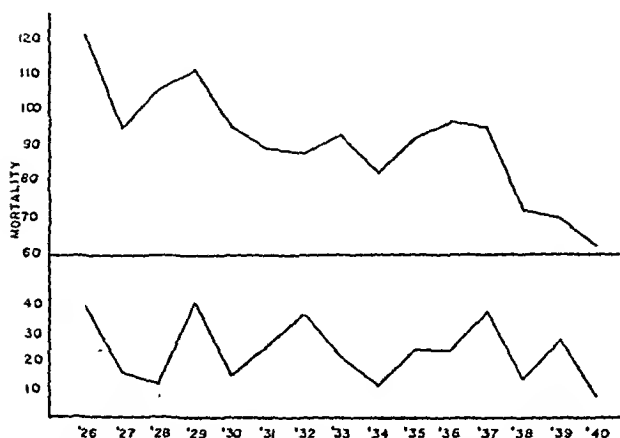


FIGURE 1. Comparison of Pneumonia Deaths and Operative Mortality in Cases of Perforated Ulcer.

The upper curve shows the deaths from pneumonia per 100,000 population in Massachusetts; the lower curve shows the corresponding percentage mortality rates in cases of perforated ulcer at the Massachusetts General Hospital.

servations of Griswold and Antoncic,⁶ DeBakey⁷ and Henry⁸ that denizens of the respiratory tract are by far the commonest pathogenic organisms cultured from the peritoneal fluid in these cases. Our own bacteriologic studies are in accord with these observers. In 47 cultures reported positive, 38 showed either pneumococcus or streptococcus; 34 per cent of these patients died, while only 7 per cent of those whose peritoneal cultures were reported as negative succumbed after closure of their perforation. It is in this group with positive cultures of virulent organisms that more modern methods of treatment by chemotherapy are apt to be effective. It will be surprising if the next report from our clinic on this subject fails to show a substantial decrease in the mortality rate.

Diagnosis in our group was rarely difficult. The history of previous indigestion is of importance, but there were a number of perforated ulcers in patients who had never been aware of any digestive disorders. Doubtless a better understanding regarding the so-called "silent" or painless area present in the duodenums of a great many people will lead to prompter diagnosis and treatment in such cases. The suddenness of the onset, with shock producing pain, localized in the epigastrium, should challenge every physician to suspect the diagnosis until disproved. Too often the onset of perforation is confused with gallstone colic, acute indigestion or angina, and the admis-

sion of the patient to a hospital is delayed for a dangerous period. In the hospital, moreover, time is often wasted in getting an x-ray examination. That free air within the abdomen can be demonstrated in a large percentage of such cases has been shown in our own series, with an incidence of 72 per cent. This doubtless could be improved on by keeping the patient in an upright position for several minutes prior to the examination or by using the method of Williams and Hartzell,⁹ who advise a lateral position for x-ray examination. Our own experience has convinced us that this confirmatory evidence is seldom necessary, and we are certain that much valuable time can be lost by laying undue stress on this method of diagnosis.

Figure 2 indicates diagrammatically the incidence and mortality according to the age of the patient. A comparison with similar data^{6,7} for other series reveals a tendency for our group to contain a larger proportion of older patients. Thus, 35 per cent of our patients had passed their fiftieth birthday, whereas most other series give figures of 18

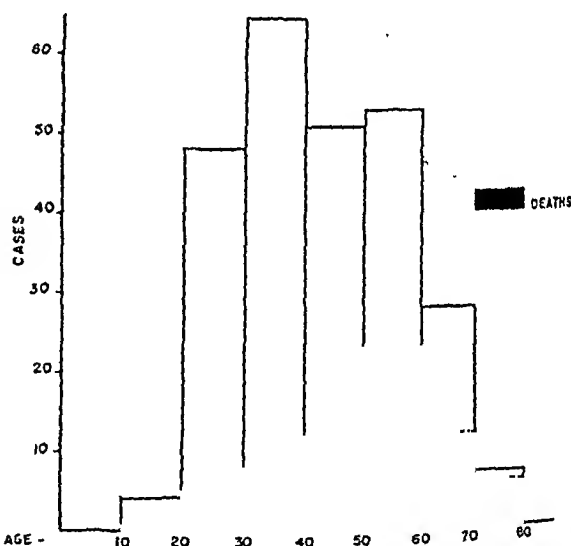


FIGURE 2. Incidences of Cases and of Deaths according to the Age of the Patient.

to 23 per cent for this subdivision. Coupled with the consideration that the mortality in these ranges is well over 35 per cent, this fact must play a significant role in the statistics for the group as a whole. Indeed, 70 per cent of all our fatalities were in the older age group. Still further causes for delay in diagnosis are met with in the patients of advanced age, since it is here that the need for excluding coronary occlusion and acute pancreatitis arises in all upper-abdominal disturbances. The time element is so important that exploratory incision under novocain should be made in cases of doubt, in preference to waiting until the diagnosis is clear.

Surgeons unanimously agree that the time interval between perforation and closure outweighs all other factors in influencing the mortality. This interval could be accurately determined in 160 of our cases and is graphically presented in Figure 3. Although at first glance it appears that a

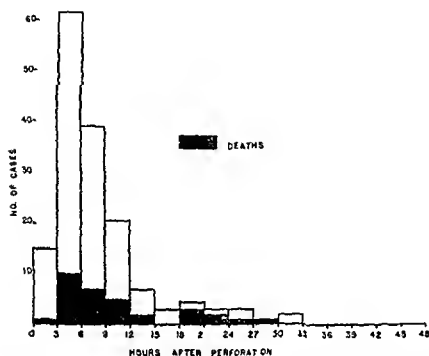


FIGURE 3 Incidences of Cases and of Deaths according to Elapsed Time between Perforation and Operation

gratifying preponderance of patients came to operation within the first twelve hours of their disease, actually the situation is much more urgent than that, for the curve of mortality with respect to elapsed time (Fig 4) shows its most rapid rise between three and six hours after perforation.

Sixteen patients came to operation between fifteen and thirty-three hours after perforation

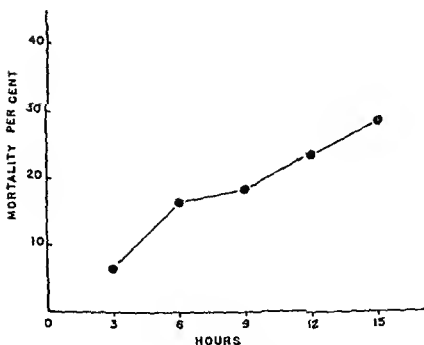


FIGURE 4 Mortality Rate according to Elapsed Time between Perforation and Operation

Nine survived, but it is of interest that those who did so had either chemotherapy (2 cases) or specific mention in the operative note that the per-

foration was found already sealed off—with one exception, a patient who had a perforation described by the surgeon as 'pin point in size'.

Twenty-five patients not shown in Figure 3 were either not operated on or came to operation forty-eight hours after perforation. Of these, 8 survived, and in all the perforation had already sealed spontaneously, as demonstrated at operation (5 cases) or by the fact that they survived without surgery (3 cases). It is probably not mere chance that no case of ours was subjected to operation between the thirty-third and forty-eighth hours after perforation. It is more reasonable to assume that spontaneous sealing, if it is to occur at all, has most frequently taken effect by twelve to fifteen hours after perforation. Patients who escape surgery until the latter part of the second day will then fall into three categories: those in whom the perforation has sealed and the improvement has been sufficient to warrant conservative treatment, those who have full blown progressive peritonitis, in whom surgery is out of the question, and those in whom the earlier peritonitis has become localized and obstruction or abscess is developing.

DISCUSSION

Patients suspected of having acute perforation of the stomach or duodenum should be hospitalized at once, and exploration should follow confirmation of the diagnosis with the least possible delay. Acute perforation ranks as an emergency second only to cessation of respiration and massive hemorrhage. A delay of only a few minutes need be expended in passing the indwelling gastric tube and starting intravenous fluid. Roentgenologic and other diagnostic aids should be reserved for those cases in which the findings will influence the decision whether or not to explore. The diagnosis *made in the recent past* has most frequently caused delay in prompt operative treatment is acute pancreatitis. Diagnostic peritoneal aspiration to determine the character of the free fluid, or even a short exploratory incision under novocain, is undoubtedly a safer and surer method of resolving this difficulty than any amount of observation and supportive treatment.

We agree with Wangenstein¹⁰ that cases seen twelve hours after onset should be examined with particular attention for signs of localization, and evaluated with reference to possible nonoperative treatment—leaning more to this course in the older age group. In the final analysis, surgery has little to offer except mechanical closure of the perforation, and should the patient be fortunate enough for this to have been accomplished spontaneously, his chances of recovery are undoubtedly

better without the added burden of anesthesia and operation. This procedure fails to consider the possibility of leakage at the site of spontaneous closure, an accident occasionally mentioned in the literature. Any estimate on the chances of this complication must await the accumulation of more data than are now at hand. With the patient on constant gastric suction and Ochsner's regimen, however, it appears to us theoretically possible to reduce the incidence of this accident to a minimum.

Anesthesia should be varied according to conditions. Proper use of local or spinal anesthesia may be advantageous. Gastric intubation and suction should precede all anesthesia, particularly if by an inhalation method. At operation, the simplest means of effecting closure is the most desirable one. This may be done by sutures in small perforations or by an omental tab held loosely over the opening as described by Graham.¹¹ Routine culture of the abdominal fluid should be taken and as much free fluid removed as can be reached with a gently manipulated suction tip, particular attention being paid to the pelvis and subdiaphragmatic spaces. Drainage of the abdominal cavity is contraindicated.

On the basis of the findings of this study, we believe that failure to use any therapeutic agent that has demonstrated its value in the treatment of respiratory-tract infections is a serious omission. Indeed, reports⁶ have already appeared describing the use of chemotherapy locally and parenterally in this disease. The postoperative use of sulfonamide compounds may be directed intelligently on the basis of the peritoneal cultures.

Postoperatively, the stomach should be kept on constant aspiration until it is apparent that there is no leakage at the point of closure, also until it is obvious that secretions meet no obstruction in the pylorus or duodenum, and until there is re-establishment of the normal peristaltic function. Parenteral fluids, vitamins, blood or plasma should be administered as indicated. The use of morphine to retain small-bowel tone is essential but

should be tempered with wisdom, lest secretions be allowed to collect in the lungs and bronchi. Tracheal aspiration, as described by Haight and Ransom,¹² should be used at once to remove troublesome bronchial exudate that the patient is unable to expectorate.

SUMMARY

Three hundred and thirty-four cases of acute perforation of gastric or duodenal ulcer were seen at the Massachusetts General Hospital in the years 1916 to 1940, inclusive.

The mortality by five-year periods shows no significant change during the past fifteen years.

The mortality during the winter months is appreciably higher than during the other seasons.

There appears to be some relation between this mortality and the virulence of current respiratory-tract infection.

The mortality rises with the patient's age.

The interval between perforation and closure is of fundamental prognostic importance.

In the majority of patients who recovered when more than fifteen hours had elapsed between onset and operation, their perforation had already spontaneously sealed.

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PAROXYSMAL TACHYCARDIA IN PREGNANCY

HENRY WEYLER, M.D.,* AND CECIL C. DUSTIN, M.D.†

PROVIDENCE, RHODE ISLAND

THERE has been some disagreement concerning the incidence of paroxysmal tachycardia in obstetric cases, and the true incidence is uncertain. Hamilton and Thompson¹ found it in 13 out of 781 patients with chronic rheumatic heart disease. However, they believe that it is found frequently during pregnancy in women who other-

The case we are presenting is of special interest because of the apparent five-year duration of the paroxysms of tachycardia, during which time the patient delivered four babies.

CASE REPORT

Mrs. A. H., a 24-year-old white woman, was under observation at the Providence Lying in Hospital during the

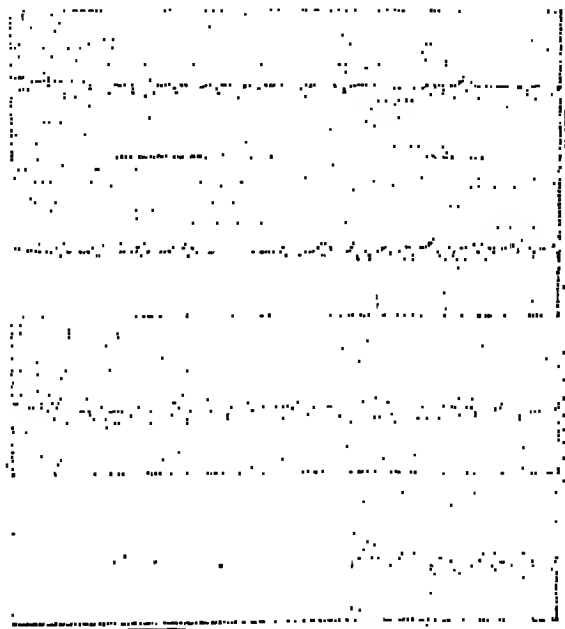


FIGURE 1. *Electrocardiogram Taken Two Months before Delivery.*

wise have sound hearts. Jensen² quotes a number of authors to indicate the conflicting opinions concerning the incidence of this condition. He concludes by saying that 19 cases have been recorded in such a manner as to leave the diagnosis beyond reasonable doubt. Eight of these had valvular disease, while 11 showed no evidence of heart disease. Browning and Clark³ described 2 more cases and published the electrocardiograms.

The past history was negative except for measles and mumps at the age of 11 years and a tonsillectomy and adenoidectomy for prophylactic reasons at the age of 5.

*Assistant visiting physician, Rhode Island Hospital, assistant cardiologist, Providence Lying in Hospital.

†Visiting physician and assistant director of the Cardiac Department Rhode Island Hospital, chief cardiologist, Providence Lying in Hospital

In particular, there was no history of rheumatic fever, chorea or sore throat. There had been no symptoms associated with hyperthyroid activity.

Physical examination showed no evidence of heart disease. A Grade 2* systolic murmur, heard during the slow

point is evident in some of the other leads, but to a lesser degree.

In the electrocardiograms made 6 weeks after the last delivery (Fig. 2) there are no runs of tachycardia. The arrhythmia is due to ectopic beats that vary considerably

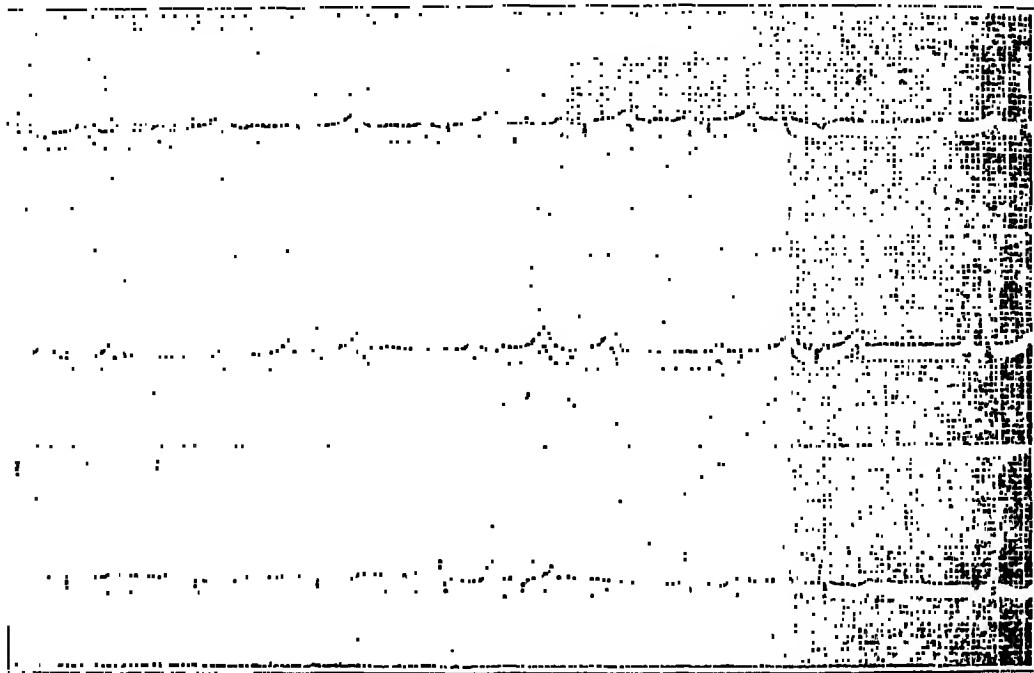


FIGURE 2. *Electrocardiogram Taken Six Weeks after Delivery.*
Note the ectopic beats in Lead 3.

beats and noted at the time of her first admission, persisted. The thyroid gland was not enlarged. The blood pressure ranged during the 5-year period from 110/69 to 122/86.

The usual laboratory findings were normal. The blood Wassermann reaction and urinalysis were negative. An x-ray examination of the heart on January 13, 1942, showed no enlargement. There was slight shifting of the heart due to scoliosis.

The electrocardiograms (Fig. 1) show a very interesting and unusual type of arrhythmia, characterized by short runs of paroxysmal tachycardia. These start with an ectopic beat and have a pause immediately following the spontaneous termination. The first complex following a run of tachycardia presumably represents the normal for the patient. In the record made before delivery, there are no places where more than two normal complexes occur in sequence. More often the slower rhythm is a coupling of a normal beat with an auricular ectopic beat. In the portions of the record showing normal complexes the rate is 64 per minute. The coupling has a rate averaging 94 per minute, and the runs of tachycardia average 140 per minute. There is only a slight variation in rate whenever the tachycardia is present.

For the most part there is very little difference in the PR interval time regardless of the type of P wave. It is evident in some of the tracings, particularly in Lead 1, that the last complex in the runs of tachycardia has a different shape of P wave than have the immediately preceding complexes. It seems that a shift in the origin of the impulse breaks up the run of tachycardia. This

point is evident in some of the other leads, but to a lesser degree. Some of these beats are definitely auricular, apparently arising near the sinoauricular node. Others are of a very different pattern, and are followed by ventricular complexes wholly unlike the normal. Lead 3 best illustrates this point. Some of the P waves are inverted, showing almost no change in the PR time as compared with the normal. These complexes have a ventricular response exactly like the normal. Other P waves are high and pointed, followed by ventricular complexes of a pattern usually associated with those arising in the ventricle. These odd complexes show a PR time that is within normal limits and almost identical with that of the normal beats. The ventricular response obviously does not follow the normal sequence.

This unusual irregularity of heart action known to have been present in this patient since her first pregnancy in 1936 has in no way interfered with her normal activity.

Attempts to control the tachycardia were unsuccessful. Small doses of digitalis were given during the last few weeks of the third pregnancy, without any effect. During the last pregnancy the patient was well digitalized, without any change in the rate or rhythm of the heart. After delivery she was given 3 gr. of quinidine sulfate[†] every 2 hours for thirteen doses. This was stopped because she complained of nausea. The electrocardiograms taken after the last dose showed a change in the pattern of the ectopic beats, with more coupling of normal and ectopic beats followed by longer runs of auricular tachycardia. The pa-

[†]Quinidine sulfate was considered during pregnancy but was not used until after delivery because we did not know its action on the uterus. There seems to be some reason for believing that the drug acts on the uterus only during labor. Browning and Clark² employed it during pregnancy and quote some authors recommending its use.

*Classification — Grades 1 to 6, according to loudness.

tient was discharged from the hospital on 3 gr. of quinine sulfate three times a day, but neglected to take it.

SUMMARY

A case of paroxysmal auricular tachycardia seen throughout the latter part of four pregnancies over a five-year period is reported.

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GOVERNOR'S ADDRESS*

ROBERT O. BLOOD, M.D.†

CONCORD, NEW HAMPSHIRE

WE ARE met here tonight at a time when more people are being maimed in the world than at any other period in its history. We had a world war once that we now call World War I, but that was only a dress rehearsal for the present conflict.

Men in the medical profession have a greater job to do the world over than has ever befallen any generation of medical practitioners in our time or in the world's history. I am sure that physicians will find themselves equal to this task, as they have in all their trials in the past years of civilized history.

We here in this state have a real job to do, and in my dual capacity—practicing medicine and at the same time being the chief executive charged by the people with the administration of the state business as a whole—perhaps I feel a little greater responsibility because of my medical background and training as it relates to medical care than a layman would in my position.

We, the State, are spending a tremendous amount of money in medical care, both as it relates to prevention and control of disease and to the care of those who are diseased. Last year we spent almost \$1,300,000 for other than the institutional care of patients. For cancer patients the State spent the sum of \$13,000, and the total expended by the Cancer Commission was over \$58,000. The State Hospital spent the sum of \$866,000 last year for the care of patients. And I may say that Dr. Dolloff, your retiring president, is running an excellent institution and that the patients are well cared for; also, the State is in a better position by having them segregated there than it would be if they were scattered about. Over 2300 patients are there now, and it is hard to predict where the care of those with mental diseases will end. The situation is a little more hopeful as it relates to tuberculosis, where we are one of the lowest nine

states in deaths per 100,000 in a year. Our rate has gone constantly down for the last twenty-odd years. However, we still annually spend the sum of \$175,000 for the care of patients in the institutions at Glenclyff and Pembroke.

If you add together all the sums I have mentioned, you will see that for the care of people in institutions, for medical care as it relates to prevention, control and so forth, we are spending a very considerable amount of money.

I believe that the medical profession is somewhat derelict in its duty in not contributing more in personnel to the legislative halls of this and other states. You have no right, unless you participate actively in the control of the legislation that is passed, to expect a layman to do too good a job. So may I leave an appeal that some of you who can go to the Legislature do so and lend a little medical influence there? It isn't a very hard job.

I want to pay my respects to the medical legislation that you have received from our legislature. I believe—and I think you will agree with me if you look over the laws as they relate to medical care, sanitary regulations and so forth—that this state will rank high among the states of the country. Changes continue to be necessary. Public health and the Board of Health activities have grown so rapidly that changes are always necessary. I told you last year that the original law, passed in 1887, said that there never should be in any one year expended for health activities more than \$3000. But from that period we have grown, slowly at first, but recently very rapidly, and the result is what you would expect it to be; we have added function after function to our health activities, and we have never "sugared them off." Re-vamping is as necessary in the State's business as it is in any other business where you add functions, one on top of another.

The medical profession might well consider learning something about our state institutions—

*An address delivered at the annual banquet of the New Hampshire Medical Society, Manchester, May 13, 1942.

†Governor of New Hampshire.

where our people who are physically and mentally ill are housed — by visiting these institutions once in a while and seeing what is being done. I think it would surprise you if you asked the men here how many of them had visited Glenclyff, Pembroke, the Laconia School and the State Hospital.

We also have a large responsibility in molding public opinion. You men have been privileged — or you could not be practicing medicine — to obtain a college education. You are marked men because of your training, and because of that, you have increased obligations with the privileges and training that you have received. There never has been a time in this state when we needed more for purposes of morale, and for purposes of as-

sistance in many ways, leadership like the leadership that you men can give in your communities.

The federal government is, of necessity, — and, we hope, wisely, — making regulations that affect every one of us. So long as those regulations are there, and so long as those regulations are fair to all of us, no one in this state will hesitate to carry on as he should.

In this war, you and I and every last one of us have a job to do, and we will contribute, we must contribute, cost what it will, — you and I in this state and the people the world over in the United Nations will contribute, — all that is necessary to defeat the Axis; for much as it costs, it will cost much less to win a war than to lose one.

MEDICAL PROGRESS

PHARMACOLOGY AND PHARMACOTHERAPY*

HARRY B. FRIEDGOOD, M.D.†

BOSTON

IN RECOUNTING strategic advances in any branch of medicine, one must take into consideration not only the new discoveries of importance, but also the welfare and aims of the field in general. Both of these depend heavily on the stimulus and guidance of men of vision who reaffirm established principles, discover new ones and adapt all of them to the ever-changing conditions of each succeeding era. Pharmacology is a science that is traditionally devoted to the study of drugs and their effects on the animal organism; but the responsibilities and interests of the pharmacologist do not end there. His ultimate concern is with the therapeutic application of the drugs whose effects he observes experimentally. Although this viewpoint enjoys universal recognition, it has not always been possible to accomplish its aim, principally because there has been altogether too infrequent professional collaboration between pharmacologist and clinician. Fortunately, there have been an increasing number of such arrangements in more recent years. In the recent passing of Dr. Soma Weiss, pharmacology has lost the genius of an internist who saw the problem of pharmacotherapy in its broadest aspects, and who contributed to it in an outstanding fashion.

Modern trends in the development of medicine leave no doubt that the field of the pharmacologist includes not only a limited study of the effects of drugs, but encompasses also an increasingly large area of the neighboring sciences of bacteriology, immunology, physiology, histoanatomy and so forth. This review, although limited in its scope, pays tribute to this important conception by including references to representative investigations in some of these fields, which meet on the common ground of pharmacotherapy.

CHEMOTHERAPY

It is scarcely possible to exaggerate the importance of the continuing advances in chemotherapy. The spotlight of interest previously monopolized by the sulfonamides is being shared more recently with reports of the bactericidal activity of gramicidin and penicillin, and with further observations on massive-dose drug therapy in early syphilis. So far as the sulfonamides are concerned, a survey of the past year's publications indicates that the topics of major interest are as follows: mode of action; use in local therapy of burns, penetrating wounds of joints, compound fractures, ophthalmologic conditions (trachoma) and cutaneous infections; prophylactic implantation of sulfanilamide in clean operative wounds; and new derivatives, principally sulfasuxidine.

Kohn and Harris^{1, 2} have studied quantitatively the growth and respiration of *Escherichia coli* in

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annals*, Vol. III, 1942 (Springfield, Illinois: Charles C. Thomas Company, 1942. \$5.00).

*From the Medical Clinic, Peter Bent Brigham Hospital, and the Department of Medicine, Harvard Medical School, Boston.

†Instructor in medicine, Harvard Medical School; associate in medicine, Peter Bent Brigham Hospital.

different mediums in the presence and absence of the sulfonamides. At the bacteriostatically active concentrations studied, the sulfonamides do not inhibit respiration of the resting or growing organism. Kohn and Harris conclude that certain substances essential to growth and multiplication are stored in the cell, and that the rate of their synthesis is inhibited by sulfonamides.

Richardson³ has investigated the small Heinz bodies, which appear within twenty-four hours after the beginning of sulfanilamide therapy in the majority of mature red blood cells. He has found that these increase in size until they reach their largest diameter by the fourth or fifth day, when blood destruction is at its peak. The occurrence of these bodies is independent of the presence or absence of changed pigment, and preliminary analyses show that they are made up of considerable amounts of cholesterol and protein and very little iron.

The idea of employing sulfonamides in the treatment of local infections and for prophylactic purposes in surgery logically follows in the wake of its successful use in systemic infections, and represents one of the major recent achievements in this field. Hooker and Lam⁴ report the successful local use of sulfanilamide powder in extensive burns, which healed rapidly and uneventfully. They were particularly impressed by the rapidity of absorption of the powder from the burned surfaces and the high blood levels that were consequently induced. Key and Burford,⁵ Long and Dees⁶ and Bickford⁷ found sulfanilamide powder highly effective in the prevention of infections in compound fractures, crushing and lacerated wounds and penetrating wounds of joints. Key and Burford⁸ and Long and Dees⁶ emphasize the prophylactic value of sulfanilamide powder locally in clean operative wounds⁹ and in any gastrointestinal surgery with soiling of the peritoneum.⁶

Keeney, Pembroke, Chatard and Ziegler¹ advocate the use of a 5 per cent sulfathiazole ointment in the treatment of cutaneous infections on the basis of a study in 69 patients with infected infantile and adult eczema, seborrheic dermatitis, impetigo, acne vulgaris, bacterial folliculitis and furunculosis. Toxic effects were not observed.

Cosgrove and Hundley¹⁰ have continued the studies of Loe,¹¹ who first reported the successful treatment of trachoma with sulfanilamide. They too are impressed with the efficacy of local therapy, and report the cure of 83 per cent of patients in the first and second stages of trachoma.¹² They also found such local therapy efficacious in gonorrheal ophthalmia, pneumococcal conjunctivitis and post-traumatic corneal ulcers.

Most recently studied of the newer sulfonamide derivatives is succinyl sulfathiazole (sulfasuxidine). It was synthesized by Miller, Rock and Moore¹³ and subsequently studied clinically by Poth and Knotts¹⁴ and Mattis and Welch.¹ Succinyl sulfathiazole exerts marked enteral bacteriostatic action, and the indications are that it will prove successful where sulfaguanidine has fallen short of its early promise. Pharmacologic studies in dogs and monkeys show that succinyl sulfathiazole administered orally has little toxicity and that it is poorly absorbed from the intestinal tract, so that only an average of 4 to 5 per cent of the ingested drug is excreted by the kidneys. Its action is essentially in the intestinal tract, as demonstrated by the reduction in the count of *E. coli* and the marked inhibition of anaerobic proteolytic bacteria, which causes the feces to become relatively odorless. Preliminary observations indicate that the dysentery bacilli, including the Shiga, Flexner and Sonne strains, are susceptible to its bactericidal action. This drug also promises to reduce greatly the hazards of intestinal surgery.

Dubos¹⁶ has opened a second front in man's fight against bacterial infection by starting with the conception that one can find in nature micro-organisms selectively adapted to the decomposition of almost every conceivable type of organic compound. He points out that like all living cells, micro-organisms carry out their biochemical functions by means of enzymes and catalysts, which can often be extracted in an active form from the bacterial cells that produce them. These catalysts show a remarkable specificity with reference to the type of reaction that they can bring about. With these considerations in mind, Dubos isolated from soil various new bacterial species that produce specific catalysts selectively adapted to protect experimental animals against certain bacterial infections. One of these agents (polysaccharidase), which is neither bacteriolytic nor bactericidal, acts by destroying the protective capsular material of pneumococci and thus renders them susceptible to the phagocytic action of the cells of the infected host. Dubos extracted the other protective agent, gramicidin, from a sporulating soil bacillus. Unlike the polysaccharidases, it does not belong to the class of enzymes, but must be regarded as a true antiseptic, minute concentrations of which inhibit the growth of susceptible species in nutrient mediums (bacteriostatic action), whereas higher concentrations actually kill bacteria (bactericidal effect). Gramicidin appears to interfere with some essential metabolic function of the invading micro-organisms. In this respect, the mechanism of its protective action presents some analogy with that of the sulfonamides. The bactericidal action of

gramicidin is in some way related to the staining characteristics of the bacterial cells. It does not affect gram-negative bacilli, and its action is apparently tied in with some as yet unidentified structural difference between gram-positive and negative cells. Dubos believes that it is not too much to hope that micro-organisms capable of attacking other types of pathogens or their toxic principles will eventually be discovered in nature.

In their experimental and clinical studies on gramicidin, Herrell and Heilman¹⁷ have observed that this substance has a powerful hemolytic effect, which renders its systemic use inadvisable. They recommend that it be used locally or in irrigating infected cavities that do not communicate with the blood stream. They used thyrothricin (the crude substance from which gramicidin is recovered) locally in the treatment of 12 cases of various types of infection with gram-positive bacteria and observed marked beneficial results in most cases without demonstrable damaging effects to the host's tissues.

The preparation of penicillin, an extract of a mold, opens a new and exciting chapter in the history of chemotherapy. An evaluation of the earliest reports on penicillin suggests that, if anything, it may have wider clinical application than gramicidin. Preliminary studies indicate that it can be given intravenously with impunity and that its use in the form of strong solutions is innocuous to tissue cells. Its bacteriostatic action in vitro resembles that of the sulfonamide drugs, with the following differences: the bacteriostatic action of penicillin against streptococci and staphylococci is much greater; the action of penicillin on these organisms, unlike that of the sulfonamides, is influenced to only a minor extent by the number of bacteria present; and in suppurating wounds, the bacteriostatic power of penicillin against these organisms, contrary to the sulfonamides, is not antagonized by hydrolytic protein breakdown products or products of tissue autolysis or pus.

The clinical experiments with penicillin are encouraging thus far, according to the report of Abraham and his co-workers.¹⁸ They administered penicillin intravenously to 6 patients with staphylococcal and streptococcal infections that had failed to respond to all previous therapy including the sulfonamides. Penicillin induced a fall in temperature and resulted in improvement of the local and general condition. The future appears to hold much that is good in store for gramicidin and penicillin and other substances of similar origin, not only from a chemotherapeutic viewpoint, but also because investigations that deal with the latter are bound to turn up collateral observations which should throw light on obscure phases of cellular

metabolism, enzyme chemistry, immunology and bacteriology.

Extensive studies on massive-dose therapy of early syphilis have been in progress for several years by virtue of a laudable co-operative experiment carried out under carefully controlled conditions in a number of widely separated hospitals. It was Ehrlich who first attempted to cure syphilis with massive doses of arsphenamine, but he abandoned the method because of unsatisfactory results. Chargin, Leifer and Hyman reintroduced the massive-dose procedure in the form of a slow intravenous drip with neoarsphenamine. The frequency of untoward reactions (especially peripheral neuritis) led them to substitute an arsenoxide, Mapharsen, for neoarsphenamine. Leifer, Chargin and Hyman¹⁹ report that 81 per cent of 334 patients with early syphilis were cured in five days by this method of treatment, and Elliott, Baehr, Shaffer, Usher and Lough²⁰ similarly found that 85 per cent of their patients in their series of 1600 cases were cured with identical therapy (1200 mg. of Mapharsen is the optimal total dose). Both groups of investigators encountered toxic encephalitis, which was a fatal complication in 0.3 per cent of the cases reported by Elliott et al. and caused cerebral symptoms without death in 1.1 per cent of the patients studied by Leifer et al. Encountered also were slight nausea, vomiting and diarrhea, which disappeared with the establishment of tolerance to the drug. Elliott and his co-workers found little evidence of liver damage and no renal damage, dermatitis exfoliativa, blood dyscrasias or nitritoid reactions in their 1600 treated cases. Although the results of these investigators are most promising, it would seem to be the better part of wisdom not to release their technic to the general practitioner until more work is done under controlled conditions with particular reference to the toxic arsenical encephalitis.

CARDIORENAL DRUGS

The bioassay of digitalis is a perennial problem in pharmacology. This past year has been no exception in this regard. Gold, Cattell, Kwit and Kramer²¹ point out that contrary to general expectation, current official methods for the standardization of digitalis do not ensure uniform potency of the drug, because the *U.S.P.* frog method of assay is not applicable to the human being. Their experiments show that when the frog and cat methods give different values for the potency of a preparation, the figure obtained by the cat method applies to human beings, whereas that obtained by the frog method does not. They have found, furthermore, that specimens that deteriorate in po-

tency with aging, as judged by the frog method, are not found similarly wanting either by the cat method or on clinical trial in human beings. More recently they²² have described a method of assay by means of which the potency of digitalis preparations can be compared in human beings, using one and the same subject and thereby eliminating errors arising from individual differences in susceptibility. Batterman, Holman and DeGraff²³ differ with Gold and his co-workers on the value of the cat method. They have studied preparations that were identical in potency according to the cat method, but weaker or stronger so far as the desired clinical therapeutic effects were concerned. They suggest the use of a mixture of constant proportions of three crystalline glycosides (lanatosides A, B and C) isolated by Stoll and Kreis from *Digitalis lanata*. None of the three satisfies the criteria for an ideal digitalis preparation, but their correct combination results in a product of known chemical composition, which they believe compares favorably in its clinical effect with *D. purpurea*. This preparation is assayed by the gravimetric method, which reinsures greater accuracy and uniformity of dosage.

A new diuretic worthy of clinical consideration, judging from preliminary observations, is the mercurated allyl succinylurea with theophylline recently reported by Nuhfer, Mellish and Buchter.²⁴ The toxicity of this solution was compared with that of Salyrgan theophylline. Ninety per cent of the dogs that were given 10 mg. of mercury per kilogram in the form of the new diuretic survived, whereas the Salyrgan preparation was fatal to 90 per cent of the dogs treated with a corresponding dose of mercury. Neither drug affected the cardiac automaticity, nor did a serious change in blood pressure result from the administration of 532 mg. of mercury per kilogram. A marked diuretic response was elicited in dogs by the preparation of mercurated allyl succinylurea with theophylline. Preliminary studies with this preparation at the Peter Bent Brigham Hospital show that an excellent diuresis can be induced in edematous cardiac patients without evidence of toxicity.

BLOOD ANTICOAGULANTS

The problems concerned with the treatment of thrombosis and the prophylactic therapy against postoperative thrombosis have been in the foreground of pharmacotherapy for some time. Heparin was naturally the first substance to be used in studies of this type. Many papers dealing with this subject have appeared during the past year or so, and for the most part the results indicate that heparin has a place in the treatment

of thrombosis and in the prophylactic care of the postoperative condition. Its probable value in embolectomy and other kinds of blood-vessel surgery is apparently even greater (Lam,²⁵ Bauer,²⁶ Murray,²⁷ Rea,²⁸ Ravdin and Wood²⁹ and Crafoord and Jorpes³⁰). An extensive review of the development of this field can be found in an article by Jorpes.³¹ Heparin has disadvantages, however, that limit its clinical usefulness; for example, it is expensive, it is effective only when administered parenterally, and its activity is of relatively brief duration. A series of well-conceived, brilliant experiments by Campbell, Roberts, Smith, Link and Overman³²⁻³⁴ were instrumental in bringing to light a new anticoagulant,—3, 3'-methylenebis (4-hydroxycoumarin),—which prolongs coagulation and prothrombin time. Their work was based on a previously recognized hemorrhagic disease in cattle (sweet-clover disease), which was described independently by Schofield³⁵ and Roderick.³⁶ The isolation and crystallization of the hemorrhagic agent were finally accomplished last year by Campbell, Link, Stahmann and Huebner.³⁷⁻³⁹ Recent preliminary communications on the clinical application of the aforementioned discoveries by Meyer, Bingham and Axelrod⁴⁰ and Butt, Allen and Bollman⁴¹ give one the impression that this principle bids fair to replace heparin for most purposes. Obviously, a great deal of clinical experimentation under carefully controlled conditions must still be done in order to substantiate the early promise of this substance and the absence of toxicity. The work thus far indicates, however, that the preparation is nontoxic; it is effective when administered orally; furthermore, it has a longer action and is cheaper than heparin.

NARCOTIC PROBLEM

The narcotic problem has come in for its share of attention during the past year. Demerol, a new analgesic drug, has been studied for its properties of addiction, tolerance and clinical effectiveness with special reference to the possibility of substituting it for morphine. Himmelsbach⁴² found that the abstinence syndrome and withdrawal symptoms were typical of, but less severe than, those induced by morphine when Demerol was given to a group of post-addicts or "recovered" patients under controlled conditions. Andrews⁴³ has observed that the pain-threshold-raising effect of Demerol, as determined by the Hardy-Wolff method, is consistently reduced, and that tolerance to this drug is similar to, but less permanent than, that developed to morphine. Batterman⁴⁴ states that Demerol has proved to be a satisfactory and safe drug in over 800 patients, most of whom would have required morphine for the relief of pain.

Slaughter, Parsons and Munal⁴⁵ have observed that prostigmin potentiates the pain-relieving action of morphine. Their observation had its origin in the work of Slaughter and Gross,⁴⁶ who found that the two drugs were synergistic in their action on the intact dog's intestine and were strikingly similar in some of their cholinergic effects. Their work shows that $\frac{1}{8}$ gr. of morphine sulfate plus 1 cc. of prostigmin methyl sulfate (1:2000 solution) acts more rapidly and is more effective than $\frac{1}{4}$ gr. of morphine sulfate alone. Furthermore, the combination affords excellent preoperative and postoperative sedation and a decreased incidence of postoperative distention and urinary retention.

DILANTIN SODIUM IN EPILEPSY AND ASTHMA

An important contribution to the treatment of epilepsy (and possibly bronchial asthma) is to be found in Dilantin Sodium.⁴⁷⁻⁴⁹ This is a drug which, with little or no hypnotic effect, prevents or greatly decreases the frequency and severity of convulsive seizures in a majority of epileptics. It is said to be much more effective in the management of seizures of the psychomotor-equivalent variety than phenobarbital or bromides. Dilantin is not recommended for patients whose seizures occur only at long intervals, unless moderate doses of phenobarbital are ineffective or induce undesirable side reactions. The great majority of toxic reactions to Dilantin Sodium occur only when large doses are employed. The gastrointestinal symptoms are chiefly nausea and vomiting, while the central-nervous-system toxicity consists of nervousness, tremor of the hands, drowsiness, headache, and ataxia. Hypertrophy of the gums and a toxic dermatitis, varying from erythema to a severe morbilliform rash, are among other toxic effects observed. Another of the toxic manifestations to which attention is being directed is the rapid and progressive fall in the blood ascorbic acid level.⁴⁸ This factor has immediate clinical importance from several viewpoints, and awaits further elucidation and evaluation. Shulman⁵⁰ has used Dilantin Sodium in bronchial asthma with encouraging results. He was stimulated to try this drug in 7 young children because of the psychosomatic aspects of the so-called "asthmatic personality."

BELLADONNA AND SYNTROPAN

A controversy over the relative merits of *U.S.P.* and Bulgarian belladonna root seems to have been settled satisfactorily. A number of investigations were stimulated by the observations of Raeff, who claimed a distinct measure of superiority for the Bulgarian belladonna plant over others in the treatment of the distressing symptoms of post-encephalitic Parkinson's syndrome. Neither Price and Merritt⁵¹ nor Fabing and Zeligs⁵² were able

to confirm Raeff's work, although the latter believe that a white-wine extract of *U.S.P.* belladonna in desiccated form (that is, pressed into tablets) is preferable to the ordinary tincture because the latter is chemically unstable and subject to deterioration.

Obstetricians will be much interested in the observations of Stoll,⁵³ who has reported that Syntropan reduces the length of labor by half if it is given when dilatation of the cervix begins. It appears to be a safe and effective method for the shortening of labor, although the pharmacologic and physiologic aspects of its effects are still unknown. Stoll believes that its effect may be related to the drug's relaxing action on the lower uterine segment or cervix.

LIPOTROPIC SUBSTANCES

According to Best, Huntsman and Ridout,⁵⁴ a lipotropic substance is one that decreases the rate of deposition and accelerates the rate of removal of liver fat. The study of these substances had fallen almost entirely within the domain of the laboratory scientist until quite recently, when Dragstedt⁵⁵ brought it to the attention of clinicians. A number of lipotropic substances have already received careful study, including choline and betaine, methionine and cystine and inositol and lipocaic. From a clinical viewpoint, Dragstedt's studies of lipocaic render it of more immediate interest than any of the other lipotropic substances. The foundations for the interesting discoveries that have been made in this field were laid in 1924 by Allan, Bowie, Macleod and Robinson.⁵⁶ They reported that depancreatized dogs receiving adequate amounts of insulin and maintained on a diet of lean meat, sucrose and bone ash did not survive for periods longer than a few months. They also found that the addition of raw pancreas to the basal diet prevented the symptoms of failure of liver function that were due to fatty infiltration of the liver. They suggested, therefore, that the pancreas might produce an internal secretion necessary for the physiologic integrity of the liver. Somewhat later it was demonstrated that egg-yolk lecithin and choline (the active agent in lecithin) could prevent the accumulation of liver fat (Best, Hershey and Huntsman⁵⁷); and Best and Huntsman⁵⁸ also found that choline could restore to a normal fat content livers of rats that had been made fatty by a high fat diet. There is considerable controversy concerning the chemical nature of lipocaic and its relation to choline and inositol. For present purposes it is sufficient to point out that lipocaic may play an important role in diabetes mellitus and arteriosclerosis. Dragstedt⁵⁵ has pointed out that two types of fatty infiltration

of the liver occur in both diabetes mellitus and experimental pancreatic diabetes. One type is due to poor control of the diabetes by inadequate insulin therapy and is characterized by a normal or high concentration of the blood lipids and acidosis; it is relieved by proper insulin therapy. The second type is due to lipocae deficiency and is characterized by a low concentration of the blood lipids, impaired liver function, decreased glucose tolerance and insulin sensitivity; it is relieved by lipocae, but not by insulin. Lipocae apparently prevents arteriosclerosis in depancreatized dogs, in which there is a greater incidence of this condition than is normal for this species. The implications of these studies are obvious when one recalls that diabetic patients are much more likely to develop presenile arteriosclerosis (coronary disease and peripheral arteriosclerosis with gangrene of the extremities) and that enlargement of the liver due to extensive fatty infiltration is not uncommon in human diabetes mellitus, particularly in children.

NUTRITIONAL ACHROMOTRICHIA

The field of vitamin therapy is too large to be included in a limited review of this type. One vitamin substance, however, which has been the subject of nation-wide publicity, merits a few words in passing. Ansbacher's⁵⁹ observations on the chromatrichial actions of *p*-aminobenzoic acid precipitated a controversy as to the nature of the gray hair factor or factors. Unna, Richards and Sampson⁶⁰ and Emerson⁶¹ were unable to attribute chromatrichial activity to *p*-aminobenzoic acid and held that pantothenic acid was the most likely source of this action. Such wide discrepancies suggested that some factor, unrecognized by either group, might be complicating the situation. With this in mind, Martin⁶² set up a series of well controlled dietary experiments on rats in which he found that six basic vitamin factors (B₁, B₂, B₆, choline, calcium pantothenate and nicotinic acid) are adequate for seemingly normal nutrition unless either *p*-aminobenzoic acid or inositol is added to the diet. He found that the addition of one of these two vitamins to the basic diet precipitated a deficiency of the other. He concluded therefore, that the *p*-aminobenzoic acid deficiency noted by Ansbacher⁵⁹ and Martin and Ansbacher⁶ was made possible by the inositol that was included in their basic diets. Neither Unna et al⁶⁰ nor Emerson⁶¹ had inositol in their basic diets, which accounts for the fact that they did not encounter a similar deficiency syndrome. Martin attributes this interdependence of vitamin substances to their effect on the bacterial growth in the gastrointestinal tract and hence on the bac-

terial synthesis of vitamin factors. Experiments such as Martin's serve to re-emphasize the complexity of the biochemistry and physiology of the vitamins. The study of these essential substances from a pharmacotherapeutic viewpoint is still more difficult because clinical experiments are less easily controlled than laboratory conditions. Martin's observations, which dovetail neatly with the experiences of other investigators, suggest that apparently innocuous chemical substances, such as vitamins, may in some circumstances induce undesirable repercussions in the body economy by upsetting what would otherwise be a biologic system in equilibrium. With this in mind, the administration of vitamin therapy to patients who show marked nutritional deficiencies should be approached with more caution than is customary, otherwise the injection or ingestion of large quantities of one or more vitamins can precipitate unrecognized subclinical deficiencies into major problems, to the great detriment of the patient. For these reasons, initial dosages are best kept within the physiologic range, and changes in metabolism should be induced gradually, not abruptly.

Martin's experiments and the experiences of other investigators indicate that there are various patterns of nutritional achromotrichia that are in some way related to the kind of vitamin deficiency that is present. This, coupled with the fact that the chromatrichial action of *p*-aminobenzoic acid is not based on simple biochemical and physiologic reactions, should put the clinician on guard against premature dogmatic conclusions with reference to any phase of this subject. In this reviewer's limited experience, there have been a few patients in whom *p*-aminobenzoic acid has shown chromatrichial activity under special circumstances; but there was also a case in which a combination of estrogen and progesterone restored prematurely gray hair of a lustrous silvery sheen to its original light brown color after several months of treatment. In this connection, the claims of Sieve⁶⁴ would seem injudicious, to say the least. With a minimum of published data, Sieve has credited *p*-aminobenzoic acid with a group of unique properties as a result of studying 800 patients in eight months. He states that this vitamin is clinically useful in a number of ways, among which are the following: it darkens gray hair; it intensifies the normal pigmentation of the nipples and mucous membranes of the mouth, vagina and anus; it eradicates areas of vitiligo; it induces a return of color and "changes the hypertrophy" of areas of leukoplakia in the mouth; it causes a decrease or almost complete disappearance of hyperpigmentation of nevi and freckles; it stimulates the libido; it re-establishes the menstrual cycle in amenorrhea.

and increases the amount of flow in oligomenorrhea; it cures female sterility (12 out of 22 cases); it benefits asthmatic patients in certain instances; and it increases the appetite and induces a feeling of well-being. Although experimental laboratory evidence indicates that *p*-aminobenzoic acid is biologically active, the list of attributes that Sieve has ascribed to this chemical substance is formidable.

ENDOCRINE PHARMACOTHERAPY

Specific knowledge concerning the biochemistry and physiology of the male sex hormones is of comparatively recent date. Testosterone was synthesized in 1935 by Ruzicka et al.⁶⁵ and by Bute-nandt and Hanisch.⁶⁶ In 1936 it was reported that organic acid esters of testosterone, such as the propionate, were more active than testosterone. The most recent advance in this field has been the development of an orally effective androgen in the form of methyl testosterone.^{67, 68}

The androgens have become increasingly important in endocrine pharmacotherapy as a result of the availability of synthetically prepared organic acid esters of testosterone. A survey of the literature discloses that there are essentially three types of male sex hormone deficiency that have been treated successfully with these synthetic androgens: hypogonadism — this group includes castrates, eunuchs, eunuchoid individuals and others who exhibit only mild symptoms of androgenic deficiency; the male climacteric syndrome; and cryptorchid prepuberal boys.

There is a unanimity of opinion in the reports of investigators who have used testosterone propionate (parenteral) and methyl testosterone (oral) in the treatment of various types and degrees of hypogonadism. Vest and Howard⁶⁹ have reported on the effects of male sex hormone therapy in several hypogonadal men. Libido was restored to 3 of the 4 men who had emissions for the first time. In all 4 cases, the testes increased in size and all symptoms of hypogonadism were ameliorated. Miller, Hubert and Hamilton⁷⁰ treated 6 impotent patients under controlled conditions (2 castrates, 2 hypogonads and 2 patients in whom impotence was probably of psychic origin). The castrates regained normal potency and personality disorders appeared to be improved in the others. Among the 54 patients treated by Turner⁷¹ were cases of hypogonadism that responded to androgen therapy with an increase in the hair growth, the penile growth, the libido and the frequency of erections and emissions. The doses of testosterone propionate used by various investigators have ranged from 15 to 150 mg. per week. Byron and Katzen,⁷² Kearns,⁷³ McCullagh,⁷⁴ Mc-

Cullagh and Rossmiller,⁷⁵ Foss,⁷⁶ Eidelsberg and Madoff,⁷⁷ Escamilla and Lissner,⁷⁸ and Wilhelm⁷⁹ observed that methyl testosterone, orally administered, is highly efficacious in the treatment of the castration syndrome and severe or moderate instances of eunuchoidism. Simonson, Kearns and Enzer⁸⁰ have made special notes on the beneficial effects of androgen therapy on the fatigue of eunuchoids and castrates. The reports from various sources cited above state that the dose of orally administered methyl testosterone is from two to six times that of testosterone propionate if one is to achieve comparable results. It has been stated that the severity of the symptoms may determine in large part the dose necessary to control the syndrome. However, it has been the experience of this reviewer, in keeping with that of Kearns,⁷³ that the more outspoken the condition, the less androgen it takes to control it and the quicker amelioration of the hypogonadism occurs.

With but few exceptions there is apparently little realization of the potential value of the synthetic androgens in the treatment of the distressing symptoms of the male climacteric. This is due mainly to the attitude of a good many physicians who have been reluctant to recognize that the male climacteric is a clinical entity. A recent editorial in the *Journal of the American Medical Association* is an official expression of this skeptical viewpoint.⁸¹ Opinions to the contrary notwithstanding, there is increasing clinical evidence of a syndrome that one may properly term the "male climacteric." The condition occurs spontaneously in men, most frequently after their fortieth year and yields satisfactorily to androgen therapy if it is properly administered. This reviewer's experience, as yet unpublished, confirms the observations of others who have described this syndrome. The latter is characterized by a lack of mental, physical and sexual drive, and may not include significant impotence in the early stages. The varied symptoms of this condition are headache, emotional instability, a tendency to periods of depression, abnormal fatigue and lassitude, impairment of memory and inability to concentrate, insomnia and occasional symptoms of vasomotor instability. It has been a not uncommon experience to find that individuals suffering from this condition go from one physician's office to another because of what appear to be intangible complaints for which an organic basis cannot be found. They finally become tagged with descriptive symptomatic diagnoses such as psychoneurosis, hypochondriasis, headache of unknown origin and even involutional melancholia.

The literature on this subject is still relatively limited. Schmitz⁸² treated 45 cases of the male

climacteric and of impotence and noted improvement in 36 of them, Donald,⁸³ who reported on a series of 50 cases of the male climacteric found that the psychologic symptoms improved first and that there was a subsequent return of mental and physical vigor. Venzmer,⁸⁴ Monetti,⁸⁵ Wolbrast,⁸ Kearns⁷³ and Finkler and Cohn⁸⁷ have observed a fairly large series of patients who were treated with either parenteral or oral androgenic therapy. They observed considerable improvement (loss of impotence, re establishment of mental and physical energy, relief from headache and vertigo and so forth). The dosage of androgen used in the treatment of these patients varied considerably (from 15 to 150 mg of testosterone propionate per week). In this reviewer's experience, an adequate dosage has been 25 mg of testosterone propionate parenterally four times per week for four to six weeks, and 30 to 40 mg of methyl testosterone* orally daily thereafter. For the time being, the only diagnostic procedure is to keep the possibility in mind when a likely case is encountered and to subject the patient to a therapeutic test.

The use of testosterone esters in the treatment of cryptorchidism or infantile genitalia in boys of the Frohlich type constitutes a relatively new departure in endocrine therapy and should be engaged in under carefully controlled conditions. It was believed until recently, because of physiologic experiments, that the administration of testosterone induced atrophy of the testes although it stimulated the growth of the penis, scrotum, seminal vesicles and prostate as well as development of pubic and axillary hair. Slay and his co-workers⁸⁸ state, however, that under certain well defined conditions immature germinal epithelium can be stimulated by testosterone propionate to increased activity. They found that the testes of treated animals contained more mature spermatozoa than those of controls. Curiously enough, they observed also that large doses of testosterone propionate caused less inhibition of growth and sperm maturation than did small doses. Jaffe and Brockway⁸⁹ report that testosterone propionate and methyl testosterone influenced favorably the growth of infantile genitalia in 5 of 7 boys. They observed the descent of a testis in only 1 of 5 cases of cryptorchidism. They also noted the increase in size of one atrophic testis. Moller Christensen⁹⁰ favors chorionic gonadotropin for the treatment of cryptorchidism, but finds that a combination of the latter with testosterone is more effective. He found that boys from twelve to fourteen years of age responded most easily. Hamilton and Hubert⁹¹ report findings in 20 true cryptorchids

(8 bilateral, 12 unilateral) who were given testosterone propionate. The testes descended satisfactorily in the 8 bilateral cases, whereas the results were only partially successful in the 12 with unilateral retention. Zelson and Steinitz⁹² and Wilson⁹³ confirm the fact that bilateral cryptorchids respond to therapy with androgens more satisfactorily than do unilateral cases. Wilson reports that 30 per cent of his cases reacted satisfactorily, and Zelson and Steinitz⁹² found that 53 per cent of their cases were treated successfully with a combination of androgens and chorionic gonadotropin. Four of the 9 boys in their series had failed to respond previously to either one or the other of these preparations alone. The reviewer's unpublished experience with this form of therapy is encouraging thus far. Six cases of cryptorchidism or infantile genitalia in which chorionic gonadotropin had failed previously to elicit a favorable response, reacted strikingly to the administration of 10 to 12 mg of testosterone propionate three times per week or 10 to 20 mg methyl testosterone orally daily. The dose had to be adjusted in each case so that neither frequent priapism nor too rapid growth of the penis occurred, both of these are commonly encountered if too much hormone is given. The testes increased in size in every instance. In 1 case, which had responded only in differently to chorionic gonadotropin over a period of eight months, the combination of the latter with testosterone propionate resulted in a rapid growth of the external genitalia and the appearance of a palpable right testicle where none had been felt previously. Boys undergoing this treatment showed an increased rate of growth and tend to lose the Frohlich type of habitus (although it is possible that judicious dieting may play an important part in the latter result).

The androgens have been used in the treatment of peripheral vascular disease, angina pectoris and benign prostatic hypertrophy. Reports of such observations are still too few and too sketchy to warrant discussion in this review.

Certain gynecologic conditions have also been treated with androgens. Reports have appeared on its use in the menopausal syndrome, dysmenorrhea, premenstrual pain in the breasts, suppression of lactation and menometrorrhagia. Salmon,⁹⁴ Silberman, Radman and Abarbanel,⁹⁵ Nicholson and Towne⁹⁶ and Kurzrok, Birnberg and Livingston⁹⁷ have reported successful results in the treatment of the menopausal syndrome with testosterone propionate. Demarest,⁹⁸ Spence⁹⁹ and others have used the androgens for the relief of premenstrual pain in the breasts. Birnberg, Kurzrok and Klor,¹⁰⁰ Siegler and Silverstein¹⁰¹ and

*The Perandren and Metandren used in these experiments were kindly furnished by the Ciba Pharmaceutical Products Incorporated, S. M. New Jersey.

Beilly and Solomon¹⁰² have observed complete inhibition of lactation with this therapy. Rubinstein and Abarbanel,¹⁰³ Geist¹⁰⁴ and others have claimed a large measure of success in the use of androgens for the relief of dysmenorrhea. The androgens have apparently been used with success in the treatment of excessive bleeding due either to uncomplicated menorrhagia, metropathia hemorrhagica or uterine fibroids, according to the reports of a number of investigators including Loeser¹⁰⁵ and more recent ones by Sturgis, Abarbanel and Nader,¹⁰⁶ Huffman,¹⁰⁷ Greenhill and Freed¹⁰⁸ and Geist.¹⁰⁴ There is considerable difference of opinion concerning the amount of testosterone propionate necessary to control so-called "functional bleeding" and the mechanism by means of which it is accomplished. Some believe that testosterone inhibits the gonadotropic activity of the pituitary and thus reduces the secretion of the ovarian hormones; others suggest that it suppresses the secretion of the ovarian hormones at their source; and it is also thought that this androgen may have a direct inhibitory effect on the intermittent rhythmic contractions of the uterine musculature, thus reducing the amount of blood flow through the uterus.

The use of androgens for the treatment of certain gynecologic endocrinopathies has not been fully justified by its protagonists to the satisfaction of most clinicians. From this reviewer's viewpoint, the best one can say for the use of testosterone in the treatment of the menopause is that it represents an interesting physiologic experiment, which may lead to information concerning the pharmacology, physiology and biochemistry of the androgens. There appears to be no justification, however, for its use clinically except in occasional cases of excessive uterine hemorrhage, because the female sex hormone is more easily obtainable, is less expensive, can be given without the risk of inducing masculinity, and is physiologically more appropriate than testosterone. As a matter of fact, it would be desirable to adopt a conservative attitude toward the use of androgens in the treatment of most of the gynecologic endocrinopathies until sufficient time has elapsed to permit a more dispassionate appraisal of the situation under controlled experimental conditions. The widespread clinical use of androgens for such purposes is to be discouraged at present, but there is little doubt that further study will more clearly define the indications for the physiologic significance of successful androgen therapy in gynecologic disorders.

Synthetic oral and parenteral preparations of progesterone are available for clinical therapy, but a perusal of the literature leaves one in some doubt about the clinical indications for its use. Theoretical-

ly, from a physiologic viewpoint, it should be helpful in a number of conditions, and on this basis it has been recommended for the treatment of recurrent and threatened abortion, functional menometrorrhagia, dysmenorrhea, amenorrhea, and premenstrual breast tenderness. Many articles have been published in support of the use of progesterone in each of these conditions, but a high percentage of them are not critical enough of the experimental conditions on the basis of which the conclusions are drawn. Take, for instance, the extensive literature on the use of progesterone in habitual or threatened abortion, much of which is reviewed by Kotz, Parker and Kaufman.¹⁰⁹ With the exception of Campbell and Sevringhaus,¹¹⁰ investigators of this phase of the subject, including Kotz and Parker, have claimed successful results with progesterone although they have routinely administered vitamin E and thyroid to each of their patients. The well-known salutary effects of each of these substances in habitual abortion are ignored for no apparent reason. Furthermore, the relatively small doses of 1 or 2 rabbit units of progesterone per week used by Campbell and Sevringhaus leave one wondering whether other factors did not have as much to do with the success they had in the handling of their cases. There is apparently no question that the percentage of patients who suffer from habitual or threatened abortion can be significantly decreased by an intelligent program that takes a number of pertinent factors into consideration, but to credit progesterone with each success would appear to be undesirable from a theoretical as well as a practical viewpoint.

Diethylstilbestrol, endocrine only through the courtesy of the physiologist, is a drug about which there is considerable controversy. It and the natural estrogens are not identical pharmacologically. Reynolds and Foster¹¹¹ have observed that even large doses of diethylstilbestrol do not cause an increase in the acetylcholine content of the uterus, whereas this does occur with the natural estrogens. In addition, DeWit and Bretschneider¹¹² have found that the drug does not cause the ovipositor reaction in female bitterlings, even when present in the water in lethal concentrations. Furthermore, diethylstilbestrol appears to be metabolized somewhat differently from the natural estrogens. The latter are largely destroyed in the liver, whereas the former is less affected by this organ and is eliminated to a much greater extent in the excreta, principally the urine (Zondek and Sulman¹¹³ and Stroud¹¹⁴).

Advocates of the relative harmlessness of diethylstilbestrol point with complacent satisfaction to the well-recognized fact that the nausea, vomit-

ing and dizziness of certain so called "sensitive persons" often disappear if therapy is continued in spite of these unpleasant symptoms. Forgotten is the additional fact that any toxic substance (for example, arsenic or nicotine) acts in a similar fashion. That is, a tolerance is built up that masks the objectively undesirable features of the drug. It should also be recalled that these toxic effects are induced by parenterally, as well as by orally, administered, stilbestrol. This indicates that the toxic effect is central. How much subtle damage (or lack of it) diethylstilbestrol may do over a period of years is as yet unknown, but in spite of this uncertainty too much of this drug is being prescribed without sufficient clinical indication just because it is relatively inexpensive and easy to obtain. Fortunately, the use of the natural estrogens has been curtailed for quite the opposite reasons.

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A review such as the foregoing is necessarily limited by the author's experience as well as by the extensiveness of the field. Nor has been made to include a discussion of all the contributions to each of the subjects that has been entertained. It is to be hoped that many of the important advances have been accounted for

370 Commonwealth Avenue

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**CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL**ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor***CASE 28471****PRESENTATION OF CASE**

A fifty-year-old machine-shop foreman was admitted to the hospital because of back pain.

Approximately three months prior to admission the patient noted occasional "twinges" of aching pain in the left lumbar region. He found that sitting slumped down in the chair afforded some relief. He also obtained moderate temporary relief from adequate doses of aspirin, which he had taken during the entire illness. The pains gradually became more frequent and severe. Nine weeks before entry, severe pains developed in the left sacroiliac region and radiated down the inner aspect of the left leg, two thirds of the way to the knee; these forced him to give up his work. He compared the pain to that of sciatica, with which he had suffered for several years. At times, however, the pain radiated into the left groin and left upper quadrant and around under the left shoulder. He slept sitting up, because he found that he had less pain in this position. There was no pain associated with bending of the trunk or flexion or extension of the legs. Three weeks prior to admission he entered a community hospital, where the x-ray studies were said to have demonstrated arthritis and a slight curvature of the spine in the lumbar region. He was fitted with a supporting belt, which was said to have afforded some relief. During the two weeks before entry he had a fever ranging between 100 and 102°F. and his ankles became swollen. During the previous nine months he was said to have lost 30 pounds and to have developed a slight degree of exertional dyspnea. His appetite was good until nine weeks prior to admission, when it fell off markedly. No abdominal discomfort occurred on a moderate diet, but when he overate he suffered with gas and sour eructations, which became progressively worse. At no time did nausea, vomiting or diarrhea develop. He had always been quite constipated, for which he took enemas or Sal Hepatica. No changes were noted in the color of the stools.

Physical examination revealed a thickset, slightly pale man who was wheezing and belching but who did not appear to be in real distress. The

heart was normal. Muscular, dry rales and wheezes were audible throughout the chest. The abdomen was moderately distended and tympanitic. There were tenderness and spasm in the left upper quadrant, which prevented careful examination of a left upper-quadrant mass that descended with inspiration. At the left costovertebral angle there was slight tenderness. There was a right mid-dorsal kyphosis and scoliosis, but the spine was flexible and there was no limitation of motion. Several fairly large hemorrhoids were felt on rectal examination. The prostate was moderately enlarged, smooth, firm and symmetrical, and was not tender.

The blood pressure was 130 systolic, 80 diastolic. The temperature was 100.5°F., the pulse 110, and the respirations 30.

The examination of the blood revealed a hemoglobin of 12.8 gm. and a white-cell count of 16,300 with 87 per cent polymorphonuclears. The urine was acid in reaction, had a specific gravity of 1.015 and gave a + test for albumin; the sediment contained a rare hyaline cast, 1 red cell and 5 white cells per high-power field. These findings were unchanged on repeated examinations. The blood Hinton test was negative. A van den Bergh was too low to read. The blood nonprotein nitrogen was 22 mg. per 100 cc., the calcium 12.7 mg., the phosphorus 2.6 mg., the phosphatase 8.1 Bodansky units, and the protein 5.1 gm. (albumin 2.6 gm. and globulin 2.5 gm.). A stool examination was negative for blood and mucus. The spinal-fluid pressure was 130 mm. (water) and the fluid contained 5 cells per cubic millimeter; the protein was 18 mg. per 100 cc., and the Wassermann test was negative. A Widal test, a heterophile-antibody test and an agglutination test for undulant fever were negative.

In an x-ray film of the chest there was mottled density in the left lower lung field and there appeared to be some pleural thickening in the left costophrenic angle; otherwise the lung fields were clear. Fluoroscopically, the changes in the left lower lung field appeared to be due to atelectasis and impaired aeration as a result of the elevated left diaphragm, which showed limitation of motion. The heart was not definitely increased in size. X-ray films of the spine showed slight degenerative changes about the lower thoracic and lumbar vertebrae; otherwise there was no definite variation from the normal. In the gastrointestinal series only a small amount of barium was given because there appeared to be considerable gas in the bowel and the patient complained of rather severe constipation. The esophagus seemed normal. The mucosa of the stomach showed no definite evidence of ulceration, but there appeared to be pressure

on the posterior wall and lesser curvature from an extrinsic mass. The duodenal loop showed no definite evidence of a constant pressure defect except that the ligament of Treitz and the proximal loop of jejunum appeared to be displaced downward by the palpable mass in this region. The spleen was not definitely enlarged. In the intravenous pyelogram the kidney outlines were not well visualized. There was an area of calcification overlying the right transverse process of the third lumbar vertebra; the calyces and pelvis on the right did not appear to be dilated. The area of calcification did not appear to be within the pelvis or ureter. There was a small amount of dye seen in the calyces on the left; the kidney appeared to be definitely displaced downward, and there was a question of a pressure defect on the superior margin of the visualized calyces. There was a small amount of barium remaining in the rectum. The bladder was not definitely abnormal.

An operation was performed on the ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. J. H. MEANS: This patient lost weight at a time when he had a good appetite. That always makes one think of thyrotoxicosis or diabetes, but as you will presently see there is no indication that this patient had either of these diseases. We are told nothing about his past history. Whether this is because it was not important or was not taken, I cannot say. In spite of the difficulty in palpating the abdomen because of tenderness, a mass was felt in the left upper quadrant but nothing much was determined about its size.

I am supposed to guess what the surgeon did and what he found.

This fifty-year-old man had a story, first, of nine months of weight loss and, then, of three months of pain, confined to his left side. The radiation suggests a phrenic-nerve distribution, possibly arising from the diaphragm. I am not sure how much of the radiation downward was due to the patient's illness on entry because he had had sciatica in the past; it is hard to tell how much of the pain was merely a continuation of that and how much was new. Apparently the patient had some difficulty in distinguishing between them. The impressive thing is that he had widespread radiation of pain both upward and downward on the left side.

On examination the most obvious thing is a mass in the left upper quadrant, which was apparently inflammatory, at least in part, because it was tender and gave rise to spasm both anteriorly and in the costovertebral region. This mass descended with inspiration. There was also some blood chem-

istry that requires careful consideration, which I shall take up a little later, but at the moment I shall ask Dr. Holmes to give me what help he can.

DR. GEORGE W. HOLMES: I can perhaps tell you some of the things it cannot be.

DR. MEANS: I should like to learn all I can about the mass—where it is, how big it is, what shape it is, what its anatomic relations are and whether it involves the colon, kidney or spleen. I want to know if there is any evidence of tuberculosis in the chest, and all I can about the skeleton—whether there are any places giving a moth-eaten appearance that might suggest myeloma or metastatic malignant disease or tuberculosis.

DR. HOLMES: I am afraid you are going to be disappointed.

DR. MEANS: If you rule them out that would be helpful.

DR. HOLMES: I shall take the chest first. There is a definite variation from the normal in the lower left lung field that has the x-ray appearance of localized atelectasis; such a condition might be due to the fact that the diaphragm is high on this side, pushed up by the mass below. I do not believe it is tuberculosis or any other active infection.

DR. MEANS: Is there any evidence of tuberculosis elsewhere in the chest?

DR. HOLMES: No; he has thickened and rather peculiar looking lung markings in both sides of the chest.

DR. MEANS: Has he got emphysema? He had some wheezing and musical rales.

DR. HOLMES: I can say the picture is consistent with emphysema but not that he actually had it. He has the increase in anteroposterior diameter often seen in emphysema.

DR. MEANS: He probably had an emphysema, but I do not believe it is very important in the total situation.

DR. HOLMES: He has a normal-shaped heart, and no more change in the aorta than he has a right to have.

DR. MEANS: Nothing abnormal in the mediastinum?

DR. HOLMES: No.

DR. MEANS: What about the dorsal spine? Is that all right? He was fifty years old.

DR. HOLMES: The spine is not unusual for a man who has done heavy work up to the age of fifty. It is the spine you often see in old people or people with emphysema. From the films I do not believe that arthritis played a very important part.

DR. MEANS: What about the mass in the abdomen?

DR. HOLMES: In the left upper quadrant is a rather indefinite area of dullness.

DR. MEANS: What about the kidneys and spleen?

DR. HOLMES: I cannot point them out on any of these films. I cannot even be certain of the mass, but I think there is a suggestion of it.

DR. MEANS: You are not sure he has a mass?

DR. HOLMES: No; but I think he has one.

DR. MEANS: This is very helpful in a negative way. At least, I believe it is.

I had various thoughts after studying this record. Certainly there was a mass. Dr. Holmes says there probably was one, and the man who did the physical examination says there was. I must accept as fact that there was a mass. Also, this mass was definitely tender and gave rise to spasm. We may say then that there was an inflammatory mass in the left upper quadrant. It was not spleen, and I get the impression from the various facts given that it might have been attached to the kidney, although probably it was not kidney alone. Since this malady began rather insidiously with pain, followed eventually by fever, and then there turned out to be a mass in the neighborhood of the left kidney, I thought first of a perinephritic abscess. As I pursued the abscess idea farther, the possibility of subphrenic abscess on the left side occurred to me. The diaphragm was high and atelectasis had been produced. Moreover there was pain that radiated to the left shoulder blade. I found it hard, however, to reconcile this diagnosis with the pain that radiated to the groin and flank and to the inner aspect of the leg. Therefore I thought of the possibility of psoas abscess arising from spinal caries of some sort. Dr. Holmes did not find any evidence of tuberculosis in the spine. By the way, Dr. Holmes, can you tell me something about the psoas muscles? Is there any evidence of psoas involvement?

DR. HOLMES: No.

DR. MEANS: I think we can therefore dismiss the possibility of psoas abscess, but there remain those of perinephritic or subdiaphragmatic abscess. What other possibilities are there? Could he have had anything arising from the splenic flexure of the colon? I suppose he could, but I do not know precisely what.

DR. HOLMES: There is pretty good evidence that there is no intrinsic disease of the colon.

DR. MEANS: Dr. Holmes says we can rule out the colon. That is very helpful.

I believe in all probability that the operation was exploration and drainage in the region of the mass. But there are a number of other points that we must consider before closing the matter.

The blood chemistry is interesting. A blood calcium of 12.7 mg. is above the upper range of

normal. The phosphorus was on the lower border of normal. The phosphatase was definitely elevated. These findings make one think strongly of hyperparathyroidism, and yet I cannot make that diagnosis with any degree of assurance. I cannot reconcile it with the rest of the picture. There is no other evidence of hyperparathyroidism — no osteitis fibrosa cystica or any kidney lesion of the sort you get in hyperparathyroidism. I think the blood findings must be due to something else.

What else could they be due to? Multiple myeloma perhaps. The calcium may be elevated in this disease. I am also told, however, that the phosphorus is usually elevated. The serum protein in this patient was 5 gm., within normal limits, but on the low side. In myeloma it is usually elevated. Furthermore, there is no other evidence of myeloma. It is a very obscure disease and sometimes turns up at autopsy, not having been suspected in life. However, I think it is unlikely here.

I was intrigued by the weight loss, which preceded the rest of the illness by six months. A progressive loss of 30 pounds certainly cannot be laughed off, and always makes one think of some disease like tuberculosis, thyrotoxicosis or cancer.

I thought of the possibility of cancer of the kidney, and I wondered if one could get suppuration secondarily. Is it fair for me to ask?

DR. MALLORY: About a month ago we had a case of a large abscess inside a hypernephroma of the kidney.

DR. MEANS: I thought of that possibility here. It probably is not that though, because I thought of it.

Lymphoma is an insidious affair that also has to be thought of. I do not believe it is, although it could be. Certainly they would not have operated if they knew it was lymphoma, and even if it turns out to have been a tumor, I believe that there must have been some inflammatory process associated with it. I think, although I am by no means certain, that there is enough evidence to make a guess that he had an accumulation of pus and that this mass was an abscess. My first choice is a perinephritic one, and my second choice subdiaphragmatic.

I am quite prepared to be told that he had a cancer somewhere, but we have no evidence of metastasis anywhere in the body to help us on that. The prostate was said to have been enlarged, but the description of it does not sound like that of malignant disease. There is nothing in the gastrointestinal tract by x-ray examination, although he did have a few symptoms pointing in that direction. I do not believe he had hyperparathyroidism. What else could give him the changes observed

in the blood chemistry? He had been immobilized to some degree in a support, and Dr. Albright has shown us that immobilization will lead to rapid osteoporosis with atrophy of disuse of the bones and an outpouring of calcium. If the kidneys are not adequate, there is a high calcium but also a high phosphorus. This patient's kidneys were all right, so I think we may dismiss such an explanation. I am at a loss to explain the blood findings, and I am not going to attempt to explain them any more than I have indicated. I am content to say that I think we shall not be told that the surgeon explored this man's neck for a parathyroid tumor, and I expect that we shall be told that the operation was for the purpose of investigating the mass in the left upper quadrant. I believe that he found a perinephritic abscess, perhaps secondary to a carcinoma of the kidney.

DR. MALLORY: Have you anything further to add, Dr. Holmes?

DR. HOLMES: I should suspect that this patient's trouble was in the region of the upper pole of the kidney,—between it and the diaphragm,—and the first thing I should think of is a tumor arising from the kidney that became infected.

CLINICAL DIAGNOSIS

Retroperitoneal tumor?

DR. MEANS'S DIAGNOSIS

Perinephritic abscess, perhaps secondary to renal carcinoma.

ANATOMICAL DIAGNOSES

Carcinoma of body and tail of pancreas, with metastases to peritoneum, liver, mesenteric and retroperitoneal lymph nodes and lung and with extension to posterior portion of stomach.

Thrombosis of splenic and left main renal veins.
Pulmonary congestion and edema, minimal.
Hydrothorax, left, minimal.

Cholecystitis, chronic.

Cholelithiasis.

Arteriosclerosis: aorta, moderate, with calcification; pulmonary artery, moderate.

Healed pyelonephritis, right.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The operation was merely a peritoneoscopy. The preoperative diagnosis was cancer in the left upper quadrant. The surgeons did not commit themselves more closely than that. The possibilities of lymphoma and carcinoma of the pancreas were mentioned. Dr. Benedict, when he looked in, saw obvious cancer implants scattered

over the peritoneal surfaces but was entirely unable to determine the primary site of the tumor.

The man went rapidly downhill, and when he came to autopsy, a huge tumor mass was found replacing the distal two thirds of the pancreas. The head of the pancreas was normal. The tumor was in such a place that it obviously did depress the duodenum, a fact that the radiologist spotted. It was large enough to have pressed on the pelvis of the left kidney, causing a little deformity, and also large enough to have elevated the diaphragm. It had invaded the serosa of the stomach but had not penetrated the muscular layers. There were extensive metastases in the liver, and one metastasis in the lower lobe of the left lung. The splenic vein was thrombosed, but the spleen was not enlarged and showed no evidence of infarction. The left renal vein was likewise thrombosed, and this kidney was enlarged, deeply congested and showed considerable tubular degeneration. The right kidney was small and deeply pitted with the scars of an old healed pyelonephritis. It is possible, therefore, that there was more renal insufficiency than was apparent from the clinical record. Unfortunately we were not informed of the chemical findings before we did the autopsy and did not investigate the parathyroid glands. The bone marrow, so far as examined, was negative.

CASE 28472

PRESENTATION OF CASE

First admission. A fourteen-month-old male child was admitted to the hospital because of generalized edema.

Two weeks prior to admission the child was found to have wet himself more frequently than usual. Ten days before, following a diarrhea for two days with loose, watery, brownish-green stools, the mother noticed puffiness about the eyes, which continued to the time of admission. Two days before, the abdomen became prominent and edema of the legs appeared. At that time, the child became "cranky." The family physician found albumin in the urine and therefore advised hospitalization.

The family and past histories were noncontributory.

Physical examination revealed a fat, fussy infant with edema about the eyes and slight edema of the lower extremities. The mucous membranes of the nose were somewhat pale and boggy. The eardrums were slightly thickened. There was some mucus in the posterior pharynx. The pharyngeal lymphoid tissue was slightly edematous. The examination of the lungs and heart was negative.

The abdomen was not prominent, and there was no edema in the abdominal wall or demonstrable scites.

The temperature was 99°F., the pulse 90, and the respirations 20.

The urine had a specific gravity of 1.040 and gave a +++ test for albumin. The sediment contained an amorphous albuminous precipitate, hyaline and fatty casts, occasional white cells and epithelial cells, and very rare red cells. The serum nonprotein nitrogen was 38 mg. per 100 cc., and the protein 3.9 gm.

On the second day the child's temperature was elevated to 101.5°F. Against advice the parents took the child from the hospital.

Second admission (four months later). The child was readmitted because of fever and diarrhea. One week before entry the patient had a slight head cold with a nasal discharge. Four days before, he fell out of the carriage, hit his head on the handle bar and had a brief nosebleed. Three days before, the child became feverish, the temperature ranging from 101 to 104°F. The next day diarrhea developed and there were as many as ten watery stools a day containing mucus and questionable small amounts of blood. During the three days of illness the patient's mother believed that the edema had diminished and that the urine volume had increased. During the twenty-four hours prior to entry, the family physician treated the patient with sulfanilamide.

Physical examination revealed a well-developed and well-nourished child who was acutely ill. He had a loose cough with some retraction of the chest with respirations. There was a contusion in the left temporal region, with some ecchymosis, and swelling about the eyes. The left eardrum was gray and shiny, with no fullness. The chest was resonant except for a questionable area of dullness at the right base posteriorly; no rales were audible. The diaphragms were high. Examination of the heart was negative. There was moderate distention of the abdomen, and a fluid wave with shifting flank dullness could be demonstrated. The child seemed to complain of pressure over the abdomen more than from a comparable degree of pressure on other parts of his body. Peristalsis was diminished. There was marked pitting edema of the scrotum and legs.

The temperature was 103°F., the pulse 123, and the respirations 20.

The examination of the blood revealed a red-cell count of 2,780,000 with a hemoglobin of 11.5 gm., and a white-cell count of 7400 with 61 per cent polymorphonuclears. The urine was acid in reaction, and had a specific gravity of 1.020, with a +++ test for albumin. The sediment contained

frequent hyaline and finely and coarsely granular casts and 8 red cells, 5 white cells and 2 epithelial cells per high-power field. The stool was brown and guaiac positive. The serum nonprotein nitrogen was 28 mg. and the sugar 108 mg. per 100 cc. The blood sulfanilamide level on admission was 7.8 mg. per 100 cc. A stool culture was negative for pathogens. An x-ray film of the skull showed no definite evidence of fracture. A chest roentgenogram revealed some density in the medial portion of the left lung. A flat plate of the abdomen showed no evidence of dilated intestinal loops.

The sulfanilamide therapy was continued. The following morning the temperature had fallen to 101°F., but the respirations were still elevated. The child was taking fluids better and urinating, and during the day two stools of normal consistence were passed. Although the pulse was rapid, the quality was good, and there was no evidence of a disturbance in the peripheral circulation. Because of the fall in temperature, it was decided to delay shifting from sulfanilamide to sulfadiazine because of the greater danger of renal irritation and of anuria associated with the latter drug. The white-cell count was 6000, and the hemoglobin 10.1 gm. The sulfanilamide level was 9.2 mg. per 100 cc. The child was given a transfusion of 250 cc. of compatible whole blood.

During the course of the afternoon the temperature rose to 103°F. and the decision was made to substitute sulfadiazine for sulfanilamide therapy. In the early evening, abdominal distention increased and a rectal tube was inserted with some results. During the night some of the distention was relieved by belching and again by the rectal tube. At 7:00 in the morning the temperature was 101°F., the pulse and respirations were still elevated and the abdomen was still distended. The child had taken fluids in sips during the night without vomiting and had just voided. At 8:30 the nurse left the room for a few moments; on returning she found the baby had vomited and had ceased breathing.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM W. BECKMAN: Certain signs are present at both admissions of this child, and, although the record does not state so specifically, I think it is safe to assume they were present in the interval between admissions. These were edema, albuminuria, cylindruria and hypoproteinemia, which constitute the most important features of the nephrotic syndrome, and I think one has to make that clinical diagnosis in this case.

The pathological diagnosis is somewhat more difficult because several types of renal pathology

have been found to be associated with the clinical entity known as the nephrotic syndrome. The first one reported was, I suppose, secondary syphilis. I do not believe that is important here for although there is no mention of any serologic test, there are no stigmas or other evidence of congenital syphilis, and nephrosis is such a very rare manifestation of syphilis that we do not have to consider it seriously.

Another not too uncommon cause of the nephrotic syndrome is intoxication with heavy metals, such as mercury. At the time of first admission one could have suspected that the child had taken mercury, unknown to the parents of course, because gastrointestinal symptoms, such as diarrhea, are typical of mercury intoxication. But a duration of four months with chronic nephrosis is too long for mercury intoxication, and we can rule it out on that basis.

The most difficult things to differentiate are the so-called "nephrotic stage" of glomerulonephritis and the "true nephrosis" of Volhard and Fahr. The only thing in favor of glomerulonephritis is the fact that there were red cells in the urine. Some writers say that if any red cells are present in the urine the diagnosis of nephrosis cannot be made. I think that is an extreme point of view, and I am sure there are published cases of true lipid nephrosis with red cells observed some time in the course of the disease. Gross hematuria is rare, but a few red cells such as this are not sufficient evidence to rule out lipid nephrosis. One datum that would be of interest and use in making the diagnosis of chronic nephritis is the blood pressure, but the pediatricians assure me that blood pressures of fourteen-month-old irritable infants are valueless. That has to be dispensed with in this case. I should also like to have evidence of nitrogen retention, as indicated by an elevated nonprotein nitrogen, to establish the diagnosis of glomerulonephritis. This child did have an elevated nonprotein nitrogen at the time of the first admission, but that could be accounted for on the basis that he probably was oliguric owing to the fact that he was forming edema at that time. The high specific gravity in the urine is further evidence of this. The nonprotein nitrogen of 38 mg. per 100 cc. was most probably due to urinary suppression. Then, on the second admission, the nonprotein nitrogen was within normal limits, whereas I should expect that, if this were chronic nephritis, the nitrogen retention would have progressed over the four months' period. So I think the best diagnosis for the underlying pathology is true lipid nephrosis. There is one prominent feature of lipid nephrosis that is not mentioned, namely, the blood lipids. In this hospital, we usu-

ally measure the cholesterol, which is elevated as all the lipids are.

DR. ALLAN M. BUTLER: It was not done.

DR. BECKMAN: That is one more constant feature of the syndrome. It may be present with chronic nephritis, but it always is with a true lipid nephrosis. I think that diagnosis explains most of the things in this case except the terminal event. Diarrhea, which was a prominent symptom, is common in nephrosis, probably owing to edema of the intestines.

The cause of the final incident must be determined. If we assume that the child had lipid nephrosis, we know that his resistance to infection was markedly diminished and certainly the terminal episode, on the basis of the fever, seems to have been infection, which is very hard to localize from the facts given in the abstract. The only lead from physical examination is that the abdomen was more tender than any other part of the body, but that is vague to say the least. There might be something in the x-ray films that would help.

DR. GEORGE W. HOLMES: I am afraid these x-ray films are not going to help much, except in a negative way. I do not see anything wrong with the chest. Some mention was made of a shadow on the left, but I do not see anything there that looks abnormal. The diaphragm is high, and the stomach is distended with gas. A film of the abdomen shows nothing remarkable and the skull films are negative.

DR. BECKMAN: Most infections in the course of lipid nephrosis are caused by the pneumococcus. No bacteriologic data are given in the record except a stool culture, which was negative, but I should guess that this infection was probably due to a pneumococcus. On the basis of the fact that the abdomen was more tender than anything else, I should say there was a pneumococcal peritonitis. That is the commonest complication and commonest cause of death in nephrosis. Usually it is one of the higher types of pneumococcus, which inhabit the normal nasopharynx and which are rarely pathogenic except in a situation where resistance to infection is greatly diminished. The normal white-cell counts throughout the course of the illness are characteristic of nephrosis. That seems to be another manifestation of the diminished resistance to infection that these patients exhibit.

The actual mechanism of death I cannot make out, but I presume it was sepsis and that the same organism found in the peritoneum was found in the heart's blood at the time of autopsy.

DR. ROBERT R. LINTON: I notice that this child had a guaiac-positive stool. Has that any significance?

DR. BECKMAN: He had frequent diarrhea, perhaps with resulting irritation.

DR. BUTLER: This child is an example of the problem of intestinal distention in patients with nephrosis. The child with nephrosis that has no infection and no anatomic cause for intestinal obstruction often has an acute bout of gastrointestinal distention, sometimes with vomiting, but almost always with refusal of food and diminished peristalsis. When this particular child entered the hospital we pictured him as one who had an acute upper-respiratory infection, possibly with a peritonitis. The question whether or not peritonitis was present seemed quite doubtful, at least from the physical findings. Peristalsis was present, formed stools were passed, and the abdominal tenderness was not definite. On the first day he seemed to improve with sulfonamide therapy and the temperature came down. We were confronted with the dilemma of using the best drug for a possible pneumococcal infection, namely, sulfadiazine, or of being satisfied with a less effective drug, namely, sulfanilamide, to lessen the chance of causing renal irritation, since one always hesitates to give sulfadiazine or sulfathiazole to a patient who is very oliguric and already has renal difficulty. When the child did not seem to be so well, we decided to put him on sulfadiazine and did. The night preceding death, when the temperature went up and the distention increased, arrangements were made with the surgical service at 7:00 a.m. to tap the child to learn further about the organism causing the peritonitis, with the idea of giving type-specific serum if indicated. In a child like this, when there is a question of peritonitis and abdominal distention, the peritoneal tap should be done as a surgical procedure, since a blind tap may perforate a loop of distended bowel. In this particular case, unfortunately, the child died before this could be done. The sudden death illustrates another point about these nephrotic children. At the Children's Hospital there have been three sudden deaths in nephrotic patients when no serious infection appeared to be present. In fact, two patients did not appear critically ill, and yet within fifteen minutes they were found dead.

CLINICAL DIAGNOSES

Nephrosis.
Acute upper-respiratory infection.
Pneumonia.
Peritonitis.
Edema and ascites.

DR. BECKMAN'S DIAGNOSES

Lipoid nephrosis.
Peritonitis (? pneumococcal).

ANATOMICAL DIAGNOSES

Lipoid nephrosis.
Peritonitis, generalized (streptococcal).
Anasarca.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This child's kidneys were greatly enlarged, weighing 200 gm., which is about three times normal. The surfaces were generally pale and smooth, but there were focal bright-yellow spots scattered irregularly over the entire cortex. On the cut surface the cortex was very pale and rather mottled. Bright-yellow streaks could be made out in the pyramids, particularly at the points where the pyramids joined the cortex. This gross appearance made it evident that there must have been a great deal of lipid in the kidneys. Microscopically they are the type of kidneys over which pathologists love to debate whether they represent a subacute glomerulonephritis or true lipoid nephrosis. There is an extremely extensive tubular damage, with much lipid in the tubules, and also many collections of lipid in the histiocytes in the stroma. There are also some obviously abnormal glomeruli—individual glomeruli can be picked out—that are quite characteristic of a true glomerulonephritis. The majority of glomeruli, however, are quite negative, except for the presence of cells that are quite distended with lipids. Sometimes the lipid deposits seem to be in the endothelial cells of the capillaries, at other times in the epithelial cells overlying the surface of the tuft. Extensive lipid deposits in the glomeruli are not, to my mind, characteristic of the early stage of glomerulonephritis. I should personally classify this kidney as a lipoid nephrosis, not as a subacute glomerulonephritis, but I am quite sure that, if I put it up to a group of twenty pathologists, there would probably be about ten on each side of the question.

The peritoneum showed 800 cc. of cloudy exudate, and culture yielded alpha and beta hemolytic streptococci but no pneumococci. We were limited at autopsy to exploration of the abdomen so we cannot say what may have been present in the heart or lungs. I have an idea that even if we had done a complete autopsy we could not have explained the sudden episode.

DR. BUTLER: Streptococcal infection is often the cause of sudden death.

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MASSACHUSETTS MEDICAL SERVICE

MASSACHUSETTS MEDICAL SERVICE — the Blue Shield — became available to the public on Monday, November 16. Hailed by all as the contribution of the physicians to the health of the people of the State during a war crisis, when every man-hour is needed on the production front, the Blue Shield is now an actuality; and the eyes of the public are focused on the profession to see whether it can live up to the high promises of an entirely new type of service.

What the public does not and cannot know is the endless time and effort that antedated the present organization of the Blue Shield. For three years a special committee appointed by the Massachusetts Medical Society, the sponsor of the plan,

studied similar projects both in this country and abroad, sifting each of them for the greatest merit. In the past few months, since the final plans were announced at the annual meeting of the Society on May 25, a large group of physicians, as well as industrial and business leaders, have given unselfishly of their time to make the Blue Shield a reality that would stand up under the test. Helping them was the State Commissioner of Insurance, who is well versed in the pitfalls of insurance practice.

There is no question that the new project will go down as history in medical annals. It will live not only for the service that it renders the public, but because the physicians of Massachusetts, despite the national crisis, were foresighted enough to offer a voluntary plan that helps to solve the growing problem concerning the equal distribution of medical care.

Massachusetts Medical Service began its operation with 2500 participating physicians. This is an impressive and adequate number, and one that foretells the success of the venture. Hundreds of additional signatures are needed, however, if the profession intends to go on record as a united group that is determined to solve medicoeconomic problems according to the principles of free practice and private initiative.

The profession can be justly proud of its achievement in launching Massachusetts Medical Service. Those who are not participants in this project, which is open to all licensed physicians in the State, should sign their applications without delay and return them to 230 Congress Street, Boston. In this manner, one hundred per cent of the physicians in Massachusetts can fulfill their role by standing solidly back of the forward-moving Blue Shield.

GASOLINE AND TIRE RATIONING

ELSEWHERE in this issue of the *Journal* is a copy of an open letter from the Gasoline Rationing Branch, Office of Price Administration, which was published in the "Medicine and the War"

section of the October 31 issue of the *Journal of the American Medical Association*.

By and large, there seems to be little need for calling physicians' attention to the things that they should do to conform to the regulations governing gasoline and tire rationing. Throughout the war effort, physicians have co-operated wholeheartedly: their response to the demands of the armed forces for medical officers has been superb; the needs of the Selective Service System and of the Office of Civilian Defense have been adequately met; and the increased activity occasioned by a depleted personnel in civilian and industrial medical practice has been cheerfully provided. Of course, as in any other group that represents a cross section of the general population, there are bound to be certain individuals who, because of carelessness, thoughtlessness or selfishness, will fail to "play the game." But these comprise a small minority, and the profession as a whole can be depended on to accept its responsibilities and to act according to standards that, throughout the years, have stood for patriotic and unselfish devotion to whatever cause, medical or otherwise, it has adopted.

MEDICAL EPONYM

SHIGA-FLEXNER BACILLUS

Kiyoshi Shiga (b. 1870), while assistant at Kitasato's Institute for Infectious Diseases, summarized his conclusions in regard to the bacillus of dysentery in an article, entitled "Ueber den Erreger der Dysenterie in Japan [The Causal Agent of Dysentery in Japan]," dated at Tokio, December 10, 1897. It was published in the *Centralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten* (Abt. I—23:599, 1898). He speaks of the failures of other investigators who had made use of animal experimentation, attributing this to the fact that most experimental animals are not susceptible to human dysentery. A portion of the translation follows:

On this account, following the suggestion of Professor Kitasato, I have investigated the subject of dysentery from another angle, namely, as follows: The question arises whether one may not find a micro-organism in the stools of patients suffering with dysentery which will show an agglutinating reaction with their blood serum, such as Widal first demonstrated with typhoid

bacilli and the serum of patients suffering with typhoid fever. I have made careful bacteriologic examinations of the stools and internal organs of 36 cases of dysentery, and have constantly found one and the same bacillus, which showed a clear-cut agglutinating reaction in the presence of serum of patients with dysentery. . . . I believe that we may probably consider this bacillus as the cause of dysentery.

He describes the cultural characteristics of the organism and further states that the serum of a person injected with the dead culture likewise shows the agglutinating reaction.

On April 12, 1900, Dr. Simon Flexner (b. 1863), professor of pathology at the University of Pennsylvania, delivered a lecture before the New York Pathological Society, entitled "On the Etiology of Tropical Dysentery." This was published in the *Bulletin of the Johns Hopkins Hospital* (11:231-242, 1900). After an exhaustive account of his investigations and a complete review of the symptomatology, bacteriology and pathology of tropical dysentery, including reference to Shiga's work, he concludes:

I think I have shown that tropical dysentery consists of a bacillary and an amebic form, separable in their early and their later stages by their clinical histories, their etiology and pathological anatomy.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

EMBOLISM

As the tabulation that appeared in the October 15 issue of the *Journal* showed, 39 cases were allocated to embolism as the primary cause of death, and this number is exceeded only by those deaths attributed to sepsis and medical causes.

Five cases were associated with cesarean section. The first was that of an elderly primipara, who after a classical section ran a slight temperature until the thirteenth day, when there were definite pain and redness in the calf of one leg. Twenty minutes later, following an attack of cyanosis and dyspnea, the patient became pulseless and expired. This embolus undoubtedly originated from a pelvic thrombophlebitis.

The second case was associated with a placenta previa. This patient had had no prenatal care until the eighth month, when she summoned a physician because of painless bleeding. The section was followed by a supravaginal hysterectomy.

Sepsis developed postoperatively; and although sulfonamide therapy was instituted and several transfusions were administered, death occurred suddenly following an acute pain in the chest on the twenty-eighth day after delivery. The supravaginal hysterectomy was done because of a very adherent placenta, which was described as an accreta.

The third case was that of a multipara who had had a marginal placenta previa diagnosed by vaginal examination; because of the resulting bleeding a cesarean section was immediately done under spinal anesthesia. Forty minutes after the beginning of the operation the patient suddenly became blue and died. This was probably an embolic death, although no autopsy was performed.

The fourth patient, who had had a previous cesarean section, died very suddenly shortly after the operation. There was no history of hemorrhage, and the diagnosis of embolism is undoubtedly correct.

The fifth case was also a repeat cesarean section, which was followed by a normal convalescence until the fourteenth day, when the patient developed a pain in her chest; three days later, while combing her hair, she slumped in the chair and died immediately. Undoubtedly this was a true case of embolism.

There were 10 cases in this series associated with operative vaginal delivery. The first occurred in a thirty-year-old multipara with twins and is an example of poor obstetrics. Labor did not start until the fifth day after premature rupture of the membranes, and attempts at forceps delivery and then at version were unsuccessful, a diagnosis then being made of a hydrocephalic baby, which was finally delivered by craniotomy. The second baby was delivered easily. Infection resulted, and in spite of sulfonamide therapy and intravenous injections of plasma, death occurred suddenly on the twentieth day after delivery. It is quite likely from the history that the infection involved the peritoneum, which suggests a possible rupture of the uterus.

The second case was associated with premature separation of the placenta, which was treated by hysterectomy. The patient was transfused four times. Infection developed, and in spite of hemotherapy, death occurred precipitately six days postoperatively. The prenatal care in this case was inadequate, the patient having been seen only once before the catastrophe; but it is doubtful whether prenatal care would have averted this fatality.

The third case was that of a patient who was delivered at home by low forceps but was moved to a hospital because of the occurrence of an em-

bolus prior to delivery of the placenta and died shortly after entry. Emboli during labor are fortunately uncommon. It is difficult to know how such a death could have been averted.

The fourth death occurred in a woman who had had six previous full-term deliveries and whose history indicated a long period of irregular bleeding. Four weeks before hospital entry a curettage had been done, the pathological report of these curetings being "necrotic placental tissue." On re-entry, because of the bleeding and the size of the uterus, which was diagnosed as a fibroid, a hysterectomy was performed and death occurred suddenly ten days postoperatively. The uterus, when opened after operation, revealed a three-month fetus. A mistaken diagnosis, of course, was the real cause of this sad catastrophe.

The fifth case was that of a patient delivered by low forceps who went into shock shortly after delivery. She was given 2 ampules of blood plasma, but death occurred shortly afterward. Post-mortem uterine palpation showed the uterus to be intact, thus ruling out rupture of the uterus. There was no history of a difficult anesthesia. Although no autopsy was performed, the suddenness of the death makes it likely that embolism was the true cause.

The sixth case was that of a multipara with six living children who, when about seven months pregnant, entered a hospital because of bleeding and presented a picture of complete separation of the placenta. The cervix was said to be dilated to admit three fingers, an easy version was done, and the patient's pulse at the end of operation was 86. Two hours post partum, however, she suddenly became cyanotic and died. It is most likely that embolism was the cause of this death because of its extremely sudden nature, but it is also possible that the version resulted in rupture of the uterus.

The seventh case was that of a multipara who suddenly became pulseless and cyanotic during labor. She was delivered by high forceps but died half an hour after delivery, and pulmonary embolism seems the most likely cause of death.

The eighth patient was an obese woman with large varicosities of the vulva and thighs who was delivered by low forceps; she died six hours after delivery, following an attack of cyanosis and respiratory distress, before a physician could get to her.

The ninth patient ran a slight temperature following a low-forceps delivery; on the eighth postpartum day a sharp pain developed in the left thigh and was followed almost immediately by cyanosis and death. This embolus was septic in origin.

The tenth case was that of a patient who had been delivered by simple low forceps nine days previous to a cholecystectomy, which was performed for an acute cholecystitis. She had an uneventful convalescence until the seventh post-operative day, when she collapsed, became cyanotic and died within fifteen minutes. Pregnancy in this case was merely incidental; death was due to pulmonary embolism following cholecystectomy.

(To be concluded)

DEATHS

GEORGE—LESLIE H. GEORGE, MD, of Haverhill died October 25. He was in his sixty-fourth year.

Born in Dorchester, he attended Clark University and the College of Physicians and Surgeons, Columbia University, and received his degree from Maryland Medical College in 1905.

Dr. George was a former member of the Massachusetts Medical Society and of the staff of Gale Hospital, Haverhill.

TUTTLE—GEORGE H. TUTTLE, MD, of South Acton, died April 2. He was in his seventy-seventh year.

Dr. Tuttle received his degree from the Harvard Medical School in 1891. He was a member of the Massachusetts Medical Society and the American Medical Association.

WAR ACTIVITIES

OFFICE OF PRICE ADMINISTRATION

GASOLINE AND TIRE RATIONING

The following open letter to all physicians of the United States was recently released by the chief of the Gasoline Rationing Branch, Office of Price Administration:

In the East Coast gasoline-rationing program, made necessary by the shortage of transportation facilities for petroleum products, the indispensability of your profession was recognized by its inclusion in the categories of persons eligible for preferred mileage, that is, necessary occupational mileage in excess of 470 miles a month. Now the Office of Price Administration has been ordered by Mr. William Jeffers to institute and administer a nationwide mileage rationing program for the express purpose of conserving our rubber-borne transportation. In framing the regulations for the new program, your profession was one of the first to be provided for.

If we are to carry out our double task of preventing a collapse of our military and civilian transportation, we must have the complete co-operation of those groups of persons whose driving is deemed essential to the war effort. Our immediate aim is to attain the 5000-mile national mileage average set by the War Relocation Authority as the maximum possible in light of the dire rubber shortage. Our experience with the East Coast program tells us that the preferred categories use one-half the gasoline consumed, though they constitute less than one-fourth the total number of automobile operators. Clearly, then, the great savings of rubber on a nationwide scale must be made in the preferred categories.

Under the regulations governing the mileage-rationing program, physicians are eligible for preferred mileage if their essential occupational needs exceed 470 miles a month and if the mileage is needed for regularly rendering necessary professional services. Mileage traveled daily or periodically between home or lodging and a fixed place of work is not considered preferred. Physicians who conduct their practices in offices, as many specialists do, are not eligible for preferred mileage.

Without question or hesitation, doctors have been and will be granted all the gasoline needed to carry out their professional work. We hope that they will regard their concrete symbol of their indispensability, the C book, as a moral obligation and not as a personal privilege. From another point of view, the C book is part of a doctor's equipment; it should not be used for anything but the work of humanity.

When nationwide gasoline rationing begins, there are certain concrete things a doctor can do to live up to the high ethical standards set for him by his own profession:

(1) At the time of first issuance of rations, he can so carefully compute his necessary mileage as to make a B book adequate for his purposes though he might easily make out a case for a C book, which might be granted to him without question by his local war price and rationing board, eager to provide for physicians.

(2) In the computation of his mileage, he can religiously adhere to the provision of the regulations, which makes 150 miles of his basic ration available for occupational purposes. Moreover, he can help mightily in establishing the principles that only 90 miles of the basic ration are to be used for home necessary use and that there is no provision whatever in any ration for pleasure driving.

(3) Conversely, if he should be granted a C book, he can return to the local board, at the end of the three-month period, all unused coupons accruing to him as a result of a quite natural overestimation of needs or of overgenerous 'tailoring' by his board instead of using such coupons for nonessential purposes. The moral effect of such an act on his fellow citizens will be incalculable.

(4) He can set an example by scrupulously observing the 35-mile speed limit, except in cases of emergency, in spite of the fact that doctors could easily get away with it.

(5) Should he be assigned to a hospital, clinic or institution after a ration card for calling on his private practice has been issued, he can use public means of transportation at the price of personal inconvenience.

(6) He can refrain from any kind of driving whatever that might appear to be nonessential in the eyes of the public.

Doctors are the leaders and molders of public opinion in their communities. If the average man has any reason to believe that the professional men whom he regards with great respect are indifferent or hostile to the mileage-rationing program, it will be difficult, if not impossible, to make it effective. Conversely, if doctors as a group observe the letter and spirit of the regulations, they will be a powerful force in making this absolutely mandatory war measure serve its purpose.

pose. We know that we can rely on the support of your profession, which has demonstrated its patriotism, ability and unselfishness at every opportunity.

JOHN R. RICHARDS
Gasoline Rationing Branch
Office of Price Administration

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1942

DISEASES	SEPTEMBER 1942	SEPTEMBER 1941	FIVE-YEAR AVERAGE*
Anterior poliomyelitis	9	66	49
Chicken pox	105	106	89
Diphtheria	11	10	9
Dog bite	870	1153	954
Dysentery, bacillary	6	110	44
German measles	69	28	21
Gonorrhea	521	403	450
Measles	150	168	127
Meningitis, meningococcal	7	8	4
Meningitis, other forms	3	2	†
Mumps	248	233	133
Paratyphoid infections	33	2	10
Pneumonia, lobar	193	106	110
Scarlet fever	316	243	155
Syphilis	460	361	408
Tuberculosis, pulmonary	276	229	243
Tuberculosis, other forms	18	23	24
Typhoid fever	4	7	10
Undulant fever	4	8	4
Whooping cough	778	546	466

*Based on figures for preceding five years.

†Pfeiffer bacillus meningitis only other form reportable previous to 1941.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Amherst, 1; Boston, 2; Fitchburg, 1; Holyoke, 1; Somerville, 1; Stoneham, 1; Weymouth, 1; Williamstown, 1; total, 9.

Diphtheria was reported from: Arlington, 1; Boston, 1; Bourne, 1; Fall River, 6; Lowell, 1; Wrentham, 1; total, 11.

Dysentery, bacillary, was reported from: Boston, 2; Lynn, 1; Salem, 3; total, 6.

Encephalitis, infectious, was reported from: Lowell, 1; Northampton, 1; total, 2.

Malaria was reported from: Arlington, 1; Boston, 1; Camp Edwards, 4; total, 6.

Meningitis, meningococcal, was reported from: Boston, 1; Cambridge, 1; Melrose, 1; New Bedford, 1; West Springfield, 1; Weymouth, 1; Worcester, 1; total, 7.

Meningitis, other forms, was reported from: Avon, 1; Plymouth, 1; Randolph, 1; total, 3.

Paratyphoid infections were reported from: Andover, 1; Boston, 11; Brockton, 1; Cambridge, 3; Framingham, 1; Greenfield, 2; Hull, 1; Mansfield, 1; Quincy, 4; Salem, 1; Somerville, 2; Walpole, 1; Waltham, 4; total, 33.

Septic sore throat was reported from: Boston, 1; Cambridge, 1; Fort Banks, 1; Ipswich, 2; Williamstown, 1; total, 6.

Tetanus was reported from: Plymouth, 1; Springfield, 1; total, 2.

Trachoma was reported from: Boston, 1; total, 1.

Typhoid fever was reported from: Arlington, 1; Everett, 1; Gloucester, 1; Pittsfield, 1; total, 4.

Undulant fever was reported from: Blandford, 1; Chatam, 1; Mattapoisett, 1; Somerville, 1; total, 4.

Weil's disease was reported from: Boston, 1; total, 1.

Communicable diseases reported at figures above their respective five-year averages were chicken pox, diphtheria, measles, meningococcal meningitis and lobar pneumonia.

Record-high figures were attained for German measles, paratyphoid infections, whooping cough and mumps. The latter, after a month's drop from record figures, is back again in the record column for the thirteenth time during the past fifteen months.

Diseases reported at figures below their five-year incidences were anterior poliomyelitis, dog bite and bacillary dysentery.

Typhoid fever and tuberculosis, other forms, were reported at record-low incidences.

Undulant fever was reported at a figure equal to its five-year average.

Two cases of animal rabies were reported from the focus in the northeastern section of the State.

CORRESPONDENCE

ROTATING INTERNSHIPS

To the Editor: To prepare physicians for war service, the members of the Medical Staff of the Salem Hospital are convinced that the rotating internship, with a knowledge of the Army and Navy requirements for young doctors, is a responsibility of hospitals today. It is not fair to a young doctor to place him in the Army or Navy without certain basic training that will enable him to meet emergency conditions that he might be called on to meet unaided.

The Salem Hospital has offered rotating internships for many years and has been accredited for the training of interns by the American Medical Association since accreditation was first offered. Both the administrative office of the hospital and its medical staff have taken this job very seriously.

Although we have endeavored to give each intern instruction and practice in all departments, eighteen months, or even two years, is too short for any of them to become expert in any one department. We have therefore tried to impress on them that if they wish to become specialists in any branch of medicine, they should seek a further internship or residency devoted exclusively to the specialty of their choice. This, many of them have done.

Now the war has changed all that, and the young doctor must get the most he can out of a one-year internship and we must see to it that he does. Whether it is worth while to help an intern through an occasional appendectomy or hernia or give him instruction in spinal anesthesia during that short service has been, and still is, a much-disputed problem. Some men react quickly and seem to profit; with others, one feels that the time spent is wasted. However, we have given them the benefit of the doubt and offered that instruction.

An incident that recently came to our notice encourages us to believe that at least during the emergency this is the right thing to do, and seems worth reporting. One of our interns who graduated last June immediately enlisted in the Navy. In due course of time, he was assigned as medical officer to a vessel and sent to sea in company with other naval ships. During the voyage, a seaman in an accompanying ship developed acute appendicitis. The medical officer of that ship had had a straight medical internship and knew little or nothing about operating. The commanding officer therefore transferred our ex-intern to that ship in mid-ocean, where he was able to give the seaman spinal anesthesia and to remove successfully the of-

adding appendix The sailor had a speedy and uneventful
nervousness

This episode is offered with all due modesty as an in-
formative rather than a laudatory message.

WALTER G. PHIPPEN, M.D., President
Medical Staff

Allen Hospital
Boston, Massachusetts

MEDICAL EDUCATION OF THE PUBLIC

To the Editor Permit me to commend you for the
and you take in relation to such articles as the one
published in *Readers Digest* regarding the one-day cure
of syphilis. There may be grave consequences from
publication of such unfinished investigations, certainly not
such good will be accomplished. Contradiction or even
discussion serves only to attract the attention of the mor-
bidly curious or innocently interested portion of the
public. However, I do not expect that your editorial nor
any feeble protest will have any effect on a magazine
which is inclined to print that brand of literature.

Married Love and Should My Boy Be Circum-
cised might be quite appropriate in a medical journal
but to my way of thinking are decidedly out of place in a
widely read and indiscriminately circulated magazine
such as the one that published them, especially one that
attempts to and seeks actively a circulation among school
children.

I know, because I have tried, how little effect criticism
has upon such publishers. As a defense, for instance, I
was informed that one of the articles was tuned so as to
appear in a summer time issue when the schools were not
in session. So I have become a trifle more circumspect
in selecting reading matter for my office as well as for my
home.

JOHN V. GALLAGHER, M.D.

Milford, Massachusetts

REPORT OF MEETING

BOSTON CITY HOSPITAL HOUSE OFFICERS ASSOCIATION

At the first of a series of meetings on war medicine,
sponsored by the Boston City Hospital House Officers
Association, Dr. Harold W. Brown, dean of the School
of Public Health at the University of North Carolina,
spoke on "Parasitic Disease Prevalent in the African and
Pacific Theaters of War."

The chief problem in the management of tropical dis-
eases is the institution of therapy at an early date to pre-
vent the otherwise chronic and disastrous sequelae of most
of these infections. The aim, then, should be to sharpen
ones diagnostic acumen in these diseases, which hereto-
fore have merely been a textbook picture to most physi-
cians. To prevent or decrease the number of cases, one
must be acquainted with the source of the infection, the
vectors involved in its transmission, and the habits of man
that make infestation possible. The problem is not con-
fined to the actual theaters of war, for these diseases on
the whole are not self limited and may be brought home
by returning troops, where they may cause disease in the
civilian population. Some parasites may even become in-

digenous in this country if the proper vector is present and
the habits of man are favorable for its perpetuation. But
many of the fears so far expressed are probably unfounded,
for most of the parasitic diseases brought back will dis-
appear through death of the parasite, host or vector.

One of the common conditions encountered in the
tropics is filariasis, most commonly caused by *Filaria ban-
crofti*. This is found in this country only in Charleston,
North Carolina, but is very prevalent in North Africa,
India, the Pacific islands and Australia. As an example,
15 per cent of the inhabitants of the Solomon Islands
have elephantiasis and many more must harbor the para-
site. Transmission is accomplished by the female of all
genera of mosquitoes, in distinction to malaria. The
microfilaria enter the blood stream and muscle of the
insect from the alimentary tract and thence migrate to the
proboscis in the course of a few weeks, where they are
ready for reinjection into the host. They are found
in the blood stream in greatest numbers and sometimes
only during the night, so smears should be taken at that
time. They require about a year to mature in the blood
stream of the host. They then find their way to the
lymph channels where they reproduce. Although many
people infected with the parasite show no symptoms, re-
current lymphangitis and elephantiasis are frequent late
manifestations. Recurrent lymphangitis may be caused
by the death of the parasites and the absorption of some
toxic substance. Elephantiasis may be initiated and cer-
tainly can be continued in the absence of any filaria. There
seems to be an original lymph stasis, which is perpetuated
in some unknown manner. Streptococcal infection may
play a major or minor role, according to various ob-
servers. Although 95 per cent of elephantiasis occurs in
the lower extremity, the scrotum, vulva and breasts are not
uncommon sites for the condition. Treatment of this
group of diseases has so far been unsatisfactory, arsenical
and mercury compounds being the drugs most widely
employed. There is some question concerning the ef-
ficacy of killing the parasites, since this may initiate either
of the late manifestations mentioned above. Although
this condition has been present in Charleston for a cen-
tury, there has been no spread, so we may be fairly con-
fident that it will not assume any great proportions in
this country.

The second large group of parasites are the schistosomes
which live in the blood vessels of man and produce symp-
toms referable to the site of predilection of each species.
Schistosomum hematobium, which invades the vessels of
the urinary bladder, is distributed widely in North
Africa, and over 50 per cent of the population of Egypt
is infected. *S. mansoni* is also found in that region as well
as in South America and some of the Pacific islands. Its
site of predilection is the liver and portal system, where it
causes ascites, various abdominal complaints and great
emaciation. *S. japonicum* is most prevalent in Japan but
is also found in certain sections of the China coast. Trans-
mission is from man to water snail to man. The eggs must
fall in water, where the miracidial form is taken up by
the snail. Here the development takes place whereby the
cercarial form is attained, and this then enters the human
host. Spines aid in the penetrating tactics of the parasites,
but there is some question whether a lytic fluid is se-
creted. The adult form lives in man, and the fact that
the eggs must fall in water may prevent the transmission
of the disease in this country. The same genus is found
here, but for some reason these snails do not seem to be
satisfactory as a vector. The conditions favoring the spread

in Asiatic and African countries, which do not obtain here, are the use of human feces for fertilizer (Asia) and defecating in or near water (Egypt).

The trypanosomes comprise one of the largest groups of pathogenic parasites. They are widely distributed in the areas where troops are now engaged in combat, and cause sleeping sickness and Chagas's disease. *Trypanosoma gambiense*, *T. rhodesiense* and so forth, which were formerly considered different, are probably the same species with various reactions dependent on the immunologic background of the host. The tsetse fly is the only known vector, and it is not found in this country; but the black (biting) stable fly of this country can mechanically transmit the parasite. Therefore the disease is possible but not very probable here. Chagas's disease, in South America, is transmitted by the *Glossina palpalis*. The cycle in the fly requires several days. Reservoirs or natural sources of these diseases are found in some antelope. Formerly as many as 50 per cent of the population of a community died each year with trypanosomiasis. The early manifestations include a rash, enlargement of the posterior cervical lymph nodes and orbital edema. At autopsy the brain usually reveals a typical nonspecific perivascular cuffing. There are two forms of treatment. The first is Bayer 205 (Germanin), which is administered intravenously. The initial dose is 0.3 gm., to test the sensitivity of the patient; if no untoward effects result, this is followed by the therapeutic dose—1.0 gm. in 10 cc. of fluid, to a total of 10 gm. There are a considerable number of reactions, some of which are fatal. Tryparsamide and other arsenicals are also employed. The former is given in a dose of 0.045 gm. per kilogram of body weight for eight to fifteen weekly injections. The main complication following the use of this drug is optic atrophy.

Other parasites commonly encountered in the tropics are the *Leishmania*. *Leishmania donovani*, found in North Africa, Asia, India and China, causes the visceral form of kala-azar. *L. tropica*, found in about the same sectors, causes a cutaneous form of the disease called Oriental sore. *L. braziliensis* also causes a cutaneous form and is prevalent in South America and even Central America. The vector is presumed to be phlebotomus, which is able to pass through most mosquito netting. It is also found in bedbugs but apparently cannot be transmitted by them. In this country the responsible mosquito is found only on Plummer's Island, off the coast of Maryland. The parasite is found in the leukocytes in man. The clinical manifestations of the visceral type are an enlarged abdomen from hepatomegaly and splenomegaly; of the cutaneous type, a chronic moist ulcer; and of the South American form, mucous-membrane lesions as well as cutaneous sores. Treatment of leishmaniasis was formerly carried out with potassium and sodium antimony tartrate, but these have now been supplanted by the pentavalent antimony compounds, such as Neostibosan. The cutaneous forms are treated by these drugs, but also receive irradiation and carbon dioxide snow.

In summary, Dr. Brown emphasized that although the habits and the lack of suitable vectors militate against endemic foci of these tropical diseases in this country, occasional cases will be brought back that have been misdiagnosed or inadequately treated. It was pointed out in passing that, although malaria is now endemic in this country in mild form, more severe forms may be brought back to plague a nonresistant host.

BOOK REVIEWS

Roentgen Treatment of Infections. By James F. K. M.D. With the collaboration of D. Arnold Dowell, M.D. 8°, cloth, 432 pp., with 122 illustrations and 25 tables. Chicago: The Year Book Publishers, Inc., 1942. \$6.00.

The title of this book suggests that it is a discussion of the roentgen treatment of all the various types of infectious process in which such treatment has been found of value. Actually its main thesis concerns the roentgen treatment of gas gangrene. To the reviewer it seems that all the pertinent facts concerning the treatment of this condition might have been clearly set forth in a treatise of some 25 pages, but instead the authors ramble through slightly more than 400 pages.

The first two chapters, amounting to about 100 pages, comprise a very elementary discussion of the early history of roentgenology, the physics of roentgenology and roentgen dosage. This discussion adds little to the value of the book.

The authors point out that the mortality from gas gangrene at the close of the last century was 50 per cent and that this rate continued through World War I: up to 1928, when roentgen treatment was first used. In their most recent series of 42 cases the rate was reduced to 5 per cent. They are opposed to the use of serum and also to the use of sulfanilamide and related compounds. They believe that débridement should be carried out only after several days of roentgen therapy, since much of the tissue that is at first discolored will later regain full vitality. The dosage recommended is about 70 r twice daily for two or three days and then once daily for several more days. The total dose rarely exceeds a threshold erythema.

There are somewhat shorter discussions of the treatment of such conditions as peritonitis, carbuncles, parotitis, mastoiditis and pneumonia.

The History and Evolution of Surgical Instruments. By Dr. C. J. S. Thompson. With a foreword by Dr. Chas. D. Leake, M.D. 4°, cloth, 113 pp., with 115 illustrations. New York: Schuman's, 1942. \$8.50.

This book is an excellent general historical survey of the surgeon's tools from the paleolithic period to the beginning of the present century. The author bases his discussion on the famous collection of surgical instruments in the possession of the Royal College of Surgeons, of which he was curator. Excellent reproductions and descriptions are given of scalpels, amputation knives, saws, trepans, vaginal dilators and speculums, head saws, artery and dressing forceps, bullet-forceps and extractors, instruments for phlebotomy and venesection, tourniquets, tractors and operating tables. The author makes special note of the famous surgeons who used these instruments.

The value of this book is measurably increased when one reads the following words: "We have suffered a grievous calamity in the almost total loss of our incomparable collection of surgical instruments at the Royal College of Surgeons. High explosives reduced the interior of the museum to ruins and the historical instruments of the museum were burnt out. It is a terrible loss as only a few specimens were saved." This book is worthy of being owned by all surgeons and should of course be in every library.

(Notices on page xiv)

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THE SEQUELAE OF WAR HEAD INJURIES (Concluded)*

D. DENNY-BROWN, M.B., D.Phil., F.R.C.P.†

BOSTON

ESTIMATION OF DEGREE OF GENERAL INJURY

Much depends on how severity of injury is defined. It soon became apparent to me that a "severe" injury is not necessarily associated with an extensive wound, laceration, depressed fracture or other surgical complication. I refer to the type of case in which unconsciousness is prolonged for a day or several days, and succeeded by confusion or delirium for many more days. Such a state is commonly called "cerebral contusion"^{32, 35} or "cerebral edema"³⁶—according to the particular theory to which the diagnostician adheres, and supported by evidence of subarachnoid hemorrhage or focal signs on the one hand, or increased cerebrospinal-fluid pressure on the other. But, with increasing experience, one soon finds that cases, such as Case 5 cited above, occur without either of these signs, or hemorrhage or increase of pressure. Furthermore, accessory methods, such as the air encephalogram, which gives very definite evidence of any local lesion, may fail to give any such indication. The injury should nevertheless be called severe. Conversely, many patients suffer epidural or subdural hemorrhage and make a rapid and permanent recovery immediately after its surgical relief. From the point of view of the persistent effect on the brain, such complications of injury must therefore be termed slight. When persistent symptoms follow relief of such a complication, the cause must be sought in some further condition—psychoneurotic, general intellectual impairment or some other.

The difficulty most writers have in accepting the entity "concussion" is that it is defined only in negative terms. If one accepts absence of contusion, edema and hematoma as its characteristics, how is one to know that a minimal degree of any or all of these entities is not present, or not de-

tectable by the relatively coarse methods of examination? The answer is twofold: concussion has been shown experimentally to occur as an *immediate* paralysis without such changes (Denny-Brown and Russell²² and Williams and Denny-Brown²³); and the electroencephalogram gives a clear indication of the presence of this condition. In traumatic coma and confusion, great slowly rolling electrical fluctuations at a rate of 1 per second occur uniformly over the entire cerebral cortex. Greatly increased intracranial pressure sometimes causes a similar state, and this possibility should be eliminated. As coma passes into confusion and delirium, faster rhythms appear. Long after the confusion has passed and normal rhythm has been established, slow undulation of the base line reflects the ground swell of the previous storm. This electrical disorder observed in my cases has been analyzed in detail and reported independently by Williams,^{11, 34} who was electroencephalographer to the hospital. The important clinical features are that the disorder is generalized (the electroencephalogram of focal contusion is focal), that it can occur without increased pressure or blood in the cerebrospinal fluid, and that it can subside at variable speeds, in from less than an hour to six months.

It is submitted, therefore, that a severe generalized disorder—for which there is at present no better name than concussion, traumatic confusion or stupor³⁷—may occur without the surgical complications that are generally described. If the progression of such coma were followed through a period of confusion lasting days, or even only one day, to recovery, one would undoubtedly rate the disturbance as severe. More difficulty arises in the interpretation of the electroencephalogram if the patient is seen for the first time months after the injury, especially when, as is common in war, accurate details of the illness are no longer available. The patient has no memory of his condition. The skull or x-ray film, or at this late date the electro-

*Presented in abbreviated form at the annual meeting of the Massachusetts Medical Society, Boston, May 27, 1942.

†Professor of neurology, Harvard Medical School; director of the Neurological Unit, Boston City Hospital; and Captain, Royal Army Medical Corps Reserve.

encephalogram, may show no objective mark of the injury or only such slight disorder as to be within the possible limits of normal variation. How, then, should the illness be judged?

The most reliable criteria found have been the duration of the post-traumatic amnesia (Russell^{16, 19}) and the defects in the intellectual status. Supporting evidence may or may not be had from the air encephalogram (dilatation of the ventricles) and electroencephalogram, depending on the time since injury.

Recently some remarks have been made deprecating acceptance of the patient's statement of his own amnesia as evidence of injury,³⁰ so far as industrial and civil accidents are concerned. Although such an objective approach to this problem is desirable, a critical questioning of the patient (particularly when he is a member of the armed forces) by a trained observer soon reveals whether his story of amnesia rings true or not, and experience in assessing large numbers of such cases has confirmed this view.

The investigation of an amnesia is too large a subject to be dealt with fully here, but the following general statements may be helpful. True concussion should be followed by retrograde amnesia, which should gradually shrink to a fixed absolute minimum. Thus, the concussed patient should not recollect the injury. The post-traumatic amnesia should not have a sharp end point, and persistent errors in judgment and difficulty in concentration should long outlast it. What the patient was told of his behavior while in the hospital should be consistent with the type of recovery known to follow a state of true confusion—for example, his inability to recognize relations or friends in spite of recovery for simple conversation. That hallucinations or manic behavior color this stage is an indication of the personality of the patient rather than of the actual nature of the injury. Thus, the trained and experienced observer will know whether amnesia is true or false. False amnesias include those of simulation and those of hysterical states. In doubtful cases, these can be recovered by treatment with Amytal or other hypnosis, whereas true traumatic amnesia cannot. If surgical complications occurred, it is essential to know whether amnesia terminated with their relief. If not, a state of general confusion may be assumed to have coexisted and undergone independent later recovery. Subject to these limitations, then, the duration of blank in memory in the mind of the patient from the time of injury onward is a very good index of the severity of generalized or concussive effect. It indicates the total duration of coma and subsequent confusion, and thus the general severity of the injury may be estimated. The

onset of the amnesic period should have been immediate. When the amnesic state had an onset at an interval after the injury, a surgical complication—such as subdural or extradural hematoma—or a hysterical episode must be suspected.

After evidence of a severe or moderately severe injury has been sought, inquiry is directed to signs of persistent damage to cerebral function. The most crucial and difficult to define is intellectual deficit. There may be a history of defects in judgment or slowness in cerebration, or of apathy since the injury. It is only to be expected that such a widespread intellectual disorder as disorientation and confusion lasting for several days or weeks should leave its mark on later intellectual function, and the clinical application of any good tests of intellectual status will define the defect. Some estimate of the intellectual level of the patient before the injury, on a basis of education and employment, must be made. In coarser degrees of deficit, tests for memory, such as digit retention, the serial subtraction of 7, test stories and general information, show marked deficiencies. In the slighter degrees of disorder, tests of judgment, the use of intelligence scales, such as the Matrix test, general tests, such as the Rorschach test, detection of absurdities and so forth, may be required to define the persistent defect.

To clarify my approach to the problem, a type of case is cited in which the injury induced a generalized cerebral disorder of relative purity (traumatic delirium or traumatic stupor). I believe that such disorder exists in some degree in all severe and many moderately severe head injuries, complicated by various combinations of contusion and edema, laceration, hematoma, subarachnoid hemorrhage, and fracture. However dangerous or alarming these complications may be immediately after the head injury, experience has shown that no one is alone responsible for long-continued disability. *The essential factor that retards or prevents full restitution of cerebral capacity is the generalized cerebral disorder*, of which the best indices are the duration of true post-traumatic amnesia and a residual intellectual deficit.

In the last thirty years, a continuous search for objective evidence of the post-traumatic cerebral syndrome has been made.¹⁸ Such criteria as increased reflexes, loss of visual convergence, change of pulse rate with posture³⁸ or with adrenalin, rise of cerebrospinal-fluid protein, slowness of cerebrospinal-fluid resorption,³⁹ persistent rise of cerebrospinal-fluid pressure^{39, 40} and, paradoxically, persistent lowering of cerebrospinal-fluid pressure⁴¹ have all had their advocates, but none have stood the test of experience. The first three listed, for example, are common in psychoneurotic states; a

high cerebrospinal-fluid protein is very seldom seen and, when present, indicates organic damage. A long-maintained, definite abnormality in cerebro-



FIGURE 7. Lance Corporal S.

This is a half-axial view of the skull of a patient who suffered intellectual impairment following a severe injury, the only other signs of which were anosmia and a crack radiating posteriorly from the foramen magnum.

spinal-fluid pressure is not found. Within two months of the injury, the spinal-fluid changes, if any, have vanished and are no longer of value in assessment. It is worth noting, however, that anosmia is frequently found as the only organic sign, associated with the severer degrees of intellectual impairment, apparently because blunt injuries, over the occiput in particular, result in severe cerebral commotion and at the same time cause tearing of the olfactory filaments. A vertical fissure in the occipital bone, radiating up from the foramen magnum and seen only in axial view (Fig. 7), may be present with the anosmia.

Ancillary methods, such as air encephalography (cisternal method) and electroencephalography, have served to clarify our ideas by lending objective evidence of damage to the cerebral structure. The second of these was used routinely, and the first in all difficult assessments and many others. Both methods suffer in their effectiveness because the slighter changes that can be thus demonstrated are also found in patients without head injury. Only rarely were they decisive in estimation of the patients who were difficult to assess by other

means. Conversely, defined change in either method alone, sometimes in both, could be consistent with successful return to duty if clinical considerations indicated it (Case 4).

Intellectual status alone is likely to give a false impression of general cerebral defect in cases in which aphasia has complicated a left-sided parietal or frontal focal lesion. Mild confusion may then impair all general intellectual function up to a late stage in recovery, but with much better ultimate prognosis than after a corresponding disturbance due to general injury. Special tests are necessary to elicit the special nature of this disturbance of function. In early convalescence, electroencephalography indicates the limited nature of

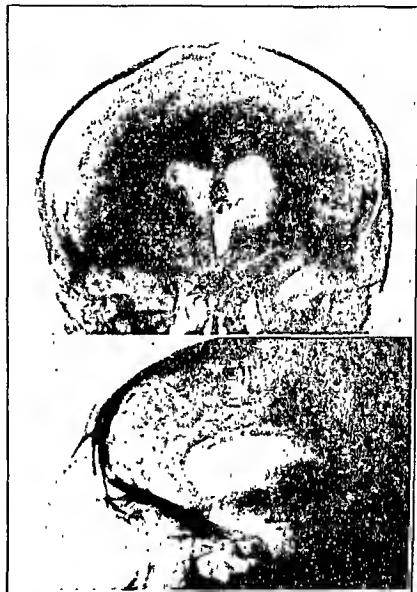


FIGURE 8. General P.

These are anteroposterior and lateral views of the skull of a patient in whom severe persistent dysphasia occurred following a blunt, nonpenetrating left temporal injury with skull fracture. Air encephalography shows a great widening of the frontal and temporal horns of the left ventricle.

brain damage in these cases, and as the localized electrical disturbance fades away, cisternal air encephalography begins to show the ventricular distortion due to the localized frontal or parietal atrophy (Fig. 8). An even, generalized dilatation of one ventricular horn caused by mild loss of brain substance following contusion (Stevenson⁴

and Greenfield⁴²) is of better prognosis than the peaked, tentlike traction defect due to an epileptogenic cerebrodural scar of the type described by Penfield.¹⁰ The former condition is by no means incompatible with return to duty, although a period of four to six months may be required before full efficiency is gained. In men and officers with long service, special qualifications and reasonably good nervous constitution, the decision that treatment should be persevered with for this period rests on a careful study made in the early stages. Such a decision in a military hospital concerns the need for avoiding the blocking of beds by patients who will never be acceptable for further duty. The accuracy of forecast in these cases depends on ability to eliminate a general intellectual defect in the presence of a focal lesion. It is necessary to distinguish the more diffuse types of dysphasia (amnesic dysphasia) from true residual aphasia, and likewise the recoverable kinds of monoparesis and hemiparesis, if accurate prognosis is to be achieved.

In thus presenting the clinical criteria on which the organic type of post-traumatic general cerebral syndrome is judged, some general considerations emerge. My experience has shown, as Symonds⁴³ had long maintained, that many patients labeled "post-concussion neurosis" or "compensation neurosis" in civil practice have in fact suffered severe cerebral injury as gauged by the above criteria. Most cases of so-called "pure traumatic neurosis" in a well-adjusted personality have been found to belong to this group.

Traumatic intellectual impairment may coexist with local cranial, facial or cerebral injury or with frank neurosis. The gravity of the general cerebral disorder in addition to such complications may have been apparent in the initial illness. Months after an injury about which adequate data are lacking, and for which the patient has a prolonged true amnesia, it may be extremely difficult to decide whether concussion did not in fact merge with contusion, hematoma, fat embolism or similar complications. Records of the duration of coma and the presence of aphasia, hemiplegia and so forth are difficult to obtain from field hospitals, but are so vital in the subsequent medical history of the soldier or airman that a special field card for head injuries was devised, with a simplified check system for rapid use in the field. The most urgent decision, however, is whether or not intellectual impairment is the substratum of the patient's present symptoms. If it is, improvement is obtained only by readjusting the patient's life to his disability.

Thus, I am not convinced that the cause of persistent organic disability lies in edema or other dis-

turbance of fluid balance, or in adhesions of meninges (epilepsy excepted). Evidence of persistent paralysis or, more commonly, of intellectual impairment, is regarded as the essential factor.

NONORGANIC FACTORS

A large group of cases with a disability syndrome that is labeled "psychoneurotic" remain to be discussed. Many of these present the post-traumatic general cerebral syndrome following trivial injury. The characteristic headache usually develops only after an interval that may be of day or longer, perhaps weeks. There is often a trace of injury, intellectual deficit, abnormal electroencephalogram or other change at any stage. A carefully taken history, however, elicits evidence of nervousness and anxiety, especially fears of serious consequences to health or to ability to continue earning.

A severe emotional reaction at the time of injury commonly occurs. Prolonged insomnia is its most reliable index. This immediate emotional reaction is not to be confused with the later emotional upheaval when, after severe injury, the patient first develops awareness of his calamity.

The disabling symptoms do not differ from other forms of anxiety neurosis except that headache is a prominent symptom. It is usually dull, generalized, steady and persistent, little or not at all relieved by rest, as in simple anxiety or depressive illness. In a small proportion of cases about one tenth, headache and dizziness on bending or on exertion, exactly comparable to those seen in the post-traumatic syndrome with severe brain damage, make their appearance. Schilder and others have suggested that the prominence of headache as a psychoneurotic reaction to head injury is related to a consciousness of the head or to ego. I believe that in the true syndrome some as yet undefined physiologic mechanism is at fault. Common association of the post-traumatic syndrome with poor physical development and with vasomotor instability, such as pallor and faints, often antedating the head injury, suggests a common background. It is remarkable that such a syndrome should respond to psychotherapy, and it is therefore concluded that it can be a psychoneurotic manifestation. Intolerance to alcohol, a well-known aftereffect of organic cerebral damage, also occurs in some purely psychoneurotic cases after trivial head injury. Headache may coexist with or be replaced by simple anxiety, fear, depression or hysterical fugues or blindness.

Psychoneurotic types of reaction to head injury are usual in mild mental defectives and psychopaths. Such persons suffer unduly prolonged disability from head injury; usually, the post-trau-

natic syndrome is a sign that their adaptation to the stresses of the world, already precarious, is easily disturbed by such an event as head injury in civilian practice, morons and aged persons are also more sensitive to disturbance of an already precarious equilibrium.

An interesting variety of the psychoneurotic type of syndrome is that seen after repeated injury, such as occurs when a dispatch motorcyclist—in peace time a performer in "dirt track" racing in which he had sustained a number of head injuries without persistent effect—breaks down following a further relatively mild head injury. The mechanism is again that of loss of adaptation to stress. A predisposed temperament, carried through a series of events by a general optimism, eventually loses adaptation following a further trauma in the face of added anxiety but no greater actual danger or damage. This is to be distinguished from the condition of one who is "punch drunk," clearly an organic syndrome of cumulative kind.

It must again be emphasized that patients suffering from true traumatic intellectual impairment may break down in a psychoneurotic manner. If the original head injury was at all severe, the greatest care must be taken to exclude this possibility. If such impairment exists, the disorder is labeled 'organic,' for although the symptoms may respond rapidly to psychotherapy, no lasting relief can be obtained without adjustment of expectations and responsibilities to the level of lowered general capacity.

Disturbances variously labeled 'black-outs' and 'loss of memory' are extremely common during convalescence from head injury, and differ in degree, from brief periods of behavior, not remembered owing to lack of concentration, to hysterical fugues, which are usually motivated by some anxiety. These disturbances are usually on a functional or psychoneurotic basis, but experience has shown that in a few cases such dissociated states were associated with true epilepsy attributable to the brain injury. Thus, traumatic epilepsy, which causes dissociation (automatism), may facilitate a motivated amnesic wandering in a patient also subject to anxiety. In such cases, the usual treatment for psychoneurosis is naturally ineffective unless the organic substructure is recognized and also receives treatment.

In Britain, the diagnosis of 'shell shock' is no longer made following the findings of a special committee in 1922,⁴⁷ and of another in 1940,⁴⁸ which recommended that the condition be resolved into its psychoneurotic or organic constituents. The common "shell shock" was none other than the psychoneurotic type of post traumatic reaction. The group also included some cases of residual intel-

lectual impairment from severe general brain injury as it is now recognized, and some of more obvious anxiety neurosis. Such disorder resulting from bomb or shell blast does, in fact, still occur, and close examination of the amnesia reveals its hysterical properties. In supposed cases of concussion due to blast, the patients turned out either to be of this type or to have suffered a secondary injury to the head from being thrown against a hard object, or struck by falling masonry, as in Eden and Turner's²⁹ cases.

The following case is an example of hysterical amnesia.

CASE 7. Private A. C. L., aged 29, survived several severe bombings without symptoms. He had an excellent family personal and occupational history. On May 30, 1940, a shell dropped within several yards of him in a trench. He remembered nothing for 3 hours, and recovered consciousness walking in a wood crying like a baby (his own words) and shaking all over, about ¼ mile behind the line. He had a severe headache but when examined at a dressing station had no sign of injury. He was transferred to a hospital, and continued to suffer from severe headaches worse in the mornings, and severe insomnia. He trembled on hearing an aircraft and kept thinking of a friend of his who had earlier been killed. The symptoms persisted and on admission under my care he was found to have no sign of injury, normal x-ray films and an excellent intellectual status. The amnesia was found under Amytal narcosis to be hysterical and with simple psychotherapy all symptoms rapidly resolved and the patient returned to duty without relapse.

The type of anxiety varies from patient to patient. In the airman, conscious or unconscious fear of further flying accidents is a natural anxiety that must always be taken into account, no matter how trivial the injury or how obvious the structural damage. The loss of an eye, or of vision in one eye conditions anxiety regarding the remaining eye. A gap in the skull, itself reasonably safe from damage, except by sharp objects, is a source of fear to the owner despite the firmest assurance to the contrary. Unreasonable fears are usually based on the gravity with which some uninformed physician has at some time viewed the scar or injury. Those who "take a grave view" and disply to the patient some uncertainty regarding the ultimate outcome, little know how lasting a fear is implanted in the patient's mind, or how disabling and difficult to treat the consequences may be. Often, the sole reason for an anxiety neurosis turns out to be some casual conversation with a friend who remarked that he knew of another who had suffered a similar injury and "never got over it." This common explanation of secondary anxieties resulting from head injury is, I am sure, the basis for the immensely superior results obtained when the convalescence from head injury is managed

throughout by a thoughtful physician well aware of the psychologic dangers besetting his patients, and when all patients with recoverable disability are early segregated from the severer ones.

With some experience, it is soon realized that a positive constitutional nervous history, in addition to a poor response to intensive, although simple, psychotherapy, will prevent any return to military duty. It is, however, often of value to have a different psychotherapist attempt treatment for a brief trial period before discharge from the service is advised, for psychotherapy is an intensely personal affair. Decision is nevertheless usually made rapidly in the severe case.

The greatest difficulty arises in the *borderline case*—the patient who makes a good response to treatment but is liable to relapse in the stress of battle. Such difficulties in England were complicated by the fact that there was no really “safe area” to which a soldier or airman could be transferred for a period. Relapse could occur as readily with bombing as with service overseas. No matter how many relatively minor or routine posts there may be in any army battalion or air-force ground staff, a man subject to relapse is always a liability to his commander. This was abundantly clear in the fighting in Belgium, where war-weary troops literally carried their neurotic comrade with them.

In the borderline cases, the critical factors in head-injury neuroses are exactly the same as those in other war neuroses with the addition of anxiety concerning the possibility of brain damage. Lewis and Slater⁴⁷ have recently studied the relation of various factors to prognosis in neurosis in soldiers, comparing two groups of 150 men, all considered by medical boards to have made full recovery. One group was successful in returning to full military duty for at least three months, the other group having been fit and returned to duty but having relapsed sufficiently to require subsequent discharge from the service. These authors list twenty attributes, which are as follows: *family history of nervous or mental breakdown*, poor school record, unsatisfactory childhood, *unsatisfactory work record*, *previous psychopathic traits or nervous breakdown or symptoms*, time in hospital, *dislike of Army life in past*, keenness to return to Army, military stress (for example, Dunkirk), adequate external anxiety (domestic or financial), disillusionment, physical factors, conversion symptoms, *querulous hypochondriasis*, depressive symptoms, anxiety symptoms, *amnesic episodes*, surly or *paranoid attitude*, fits and faints. The italicized factors are shown to operate powerfully in favor of relapse, but the analysis also shows clearly that no one of these factors is alone sufficient for unsatisfactory

return to duty; it is any combination in this series that counts. Exposure to severe military stress and keenness to get back to duty are shown to operate clearly in favor of successful return to full duty. This is entirely in accord with my own experience with head-injury neurosis. However, to the italicized group, I should add disillusionment, anxiety about brain damage and fits. The decision to return to duty in borderline cases depends on the number of these factors, their duration and the nature of the stress that precipitated them.

Much has been made of ventricular dilatation demonstrable by air encephalogram in cases of head injury since attention was first drawn to its occurrence by Bielschowsky.³⁰ It has been held to demonstrate an organic basis for psychoneurotic symptoms.^{48, 49} My experience has led to the opinion that, although it means loss of cerebral substance and damage to axis cylinders and myelin,⁵⁰ ventricular distortion by no means settles the nature of the patient's disability. As in Case 3, it is frequently present when no persistent disability has occurred, and also in many other cases in which the disability is demonstrably a psychoneurosis and is amenable to treatment. This may also be true of persistent electroencephalographic abnormality, which must be considered in relation to other factors, such as nervous constitution and intellectual impairment, before it can be regarded as significant.

It is of considerable interest to compare the conclusions reached by us with the excellent clinical analysis of civilian compensation cases made by Schaller.¹⁷ Whereas our findings agree in broad essentials with his two clinical syndromes (post-traumatic concussion state and post-traumatic psychoneurotic state), which are common and characteristic, no single clinical feature is diagnostic, and every variety of intermixture can be found. Moreover, the psychoneurotic patient is often anxious to resume occupation, and more frequently exhibits difficulty in concentration, precise symptomatology and tendency to improve than the patients in Schaller's series. Our organic cases also showed more liability to functional overlay, more frequent headache and less aggressiveness than those of Schaller. Although the extreme clinical syndromes are characteristic, no single clinical feature is diagnostic. Nor do we consider the conception of “post-traumatic general cerebral syndrome” of Foerster¹⁴ as a clinical entity of practical value. Of such a variable series of clinical pictures as those persisting from head injury, no two or three broad divisions are possible. Instead, each case should have separately estimated organic residua and psychoneurotic symptoms.

PSYCHOSIS

Frank psychosis resulting from head injury is extremely rare. Mania, deep depression or schizophrenia (1 of each in the 400 cases) may be precipitated by the general disturbance of the injury in a person with a strong predisposition. More commonly, the phase of confusion during recovery from a severe injury may be colored by elation, depression or hallucinatory experience. When confusion is prolonged, this phase may also be prolonged for weeks or months, but with a steady tendency to recovery.⁴³ A type of phonographic loquacity associated with catatonia was seen in 2 cases in this period.

Changes in personality and outbursts of irritability are not uncommon (9 in the 400 cases), but there is usually some evidence of instability and swinging of mood before the injury. Obsessional traits may become extremely pronounced. Such changes are therefore regarded as usually being psychoneurotic, and are not directly comparable to the more complete change in personality seen sometimes in children after head injury.

CULPABILITY

The greatest emphasis must be placed on the frequent combination of structural damage and psychoneurosis. It is impossible to keep these two pigeonholes entirely separate. It is both unjust and bad treatment to regard conscious or subconscious malingering as the only alternative to grave damage to the brain. Pure malingering is extremely rare, and its inconsistencies relatively easy to entrap. Psychoneurotic behavior motivated by dislike of military life is commoner. But most post-traumatic neuroses, especially the psychoneurotic factors that prolong disability from head injury, are deeper than this. Most commonly, they arise from a combination of natural anxieties with prolonged war stress. These and constitutional liabilities are beyond the patient's realization or control. Although careful psychiatric selection of draftees will minimize disorders due to constitutional psychoneurotic liability, it cannot entirely prevent them. Even in air-force pilots, very highly selected in this respect, the constitutional factor was often elicited only by prolonged investigation after the disability had arisen.

Whereas psychoneurosis has not the stigma it once had, some further education of the general lay public is necessary in this respect, for in many cases war trauma is in part or wholly responsible for prolonged total disability of psychoneurotic kind, incurred through truly courageous and heroic acts. That it should occur very often in the course of simple devotion to duty should not close one's eyes to its essential nature and thus erect a barrier

to efficient treatment. That the bravest man may develop a psychoneurosis through no fault of his own, particularly under circumstances of exhaustion and fatigue, was a fact well recognized as long ago as 1815 by Lord Wellington when he was consulted regarding a psychoneurotic casualty of the Peninsular War.⁵¹

When compensation is a factor, the issue should be fairly and squarely faced and decided forthwith. Compromise in this respect nullifies the effect of any kind of treatment. Once the issue is settled, in service as in civil cases, treatment should proceed, for the condition seldom subsides spontaneously.

TREATMENT

From what has been said, it should be clear that head injury is by no means a clinical entity for which a cut and dried line of treatment can be prescribed. This is as true of the persistent after-effects as of the acute stages. Each case must be treated according to its particular merits. When the relative gravity of bony, cerebral and emotional factors and the effect of any foreign bodies that may be present have been estimated, the line of treatment to be pursued and its likelihood of success become clear.⁵² Objective records, such as ventricular air studies and electroencephalography, are extremely valuable but seldom achieve a short cut to clinical evaluation.

It is not considered possible even to list a particular treatment for any particular symptom, for any symptom may have either psychoneurotic or organic emphasis and, if organic, a focal or generalized cause. Thus, traumatic epilepsy may be related to a transient effect of a single defined scar or diffuse degenerative process, may have an identifiable removable cause, or may be only the awakening of a latent liability by a generalized physical effect. This is also true of paralysis, or visual disorder, when only experienced, trained observers can give an estimate of the degree of unrecoverable disability. It is not enough to say that a patient cannot read because he has a visual-field defect. One must know whether that particular defect does in fact interfere with reading and, if so, whether a particular method of training can bring improvement, and if not, how to deal with the psychologic difficulty that blocks recovery. In the armed forces, it is further necessary to be able to give some estimate of the prognosis regarding ultimate resumption of duty, and the time likely to be consumed. The problem is then often complicated by the fact that the limitation in capacity may not enable the patient to continue holding his former appointment, and intimate knowledge of the service is required to determine whether such limi-

tation is possible in other duty carrying the same rank, and, if not, whether the necessary change in status is likely to be the cause of a relapse.

The treatment of surgical complications is one of which the neurosurgeon can more properly speak. For all types of organic paralysis, such as spasticity, loss of sensation and of vision, and ataxia, exercises are more valuable than any other form of therapy and, in addition to experience, enthusiasm and adaptability are of the greatest benefit in the physiotherapy division. Enough has been said to indicate that even the most apparent spastic hemiplegia should be carefully assessed for psychoneurotic and other complicating features before it is assumed that no further recovery is possible.

Psychologic treatment is most effectively undertaken and supervised by those who take the original psychiatric history, for the initial psychologic rapport and understanding thus obtained is a good starting point. For hysterical amnesia, hypnosis and prolonged association are effective but time consuming, and most experienced workers shorten the procedure with brief Amytal narcosis, to break down inhibitions and take a short cut to suggestive treatment. All anxieties are fully discussed, and reassurance given. Encouragement and supervision in graded occupation and exercise are necessary. Communication with the soldier's commanding officer may be needed in matters of pay or discipline, and with the Red Cross or other social services or relatives for the patient's family troubles.

All cases of structural injury to the brain and skull require such prolonged convalescence that, unless some interesting diversion is provided, psychoneurotic complication or ordinary discouragement is liable to occur. Here is the place for occupational therapy, — leatherwork, basket making, bookbinding, wood carving and so forth, — which was early developed in our hospital and assumed a most important place in therapy. It should not be confused with rehabilitation, and nothing is worse than for these patients to get the idea that organized carpentry is to refit them for civilian life. They should recognize from the first that they are to return to duty, and should regard the treatment as a pastime. The best instructor gives most time to the clumsy performer, for it is he who is deriving most benefit. Others are apt to spend too much time with their more successful pupils, forgetting that they either no longer require instruction or should be promoted to more strenuous activity. The subject has recently been discussed by Jefferson et al.⁶³

For the final stages of convalescence, a rigorous schedule is required. This was carried out in a special convalescent branch of the hospital with a resident medical officer. There was also a weekly visit and an interview of each patient by the med-

ical specialists of the parent hospital. Graded physical activity and exercise, especially stooping, leading up to heavy digging, sawing wood, swimming, football and boxing, were essential. Only in this way could a disappointing relapse be prevented on return of the soldier to active military duty.

Throughout this performance, it is essential for a physician who knows the whole circumstances of the case to supervise progress. Time must be given to regular discussion of all problems with each patient. Only then is it realized how small problems crop up from day to day, and how much individual attention to detail counts. And this extends, as will be explained below, to the personal and family affairs of the man.

The medical officer soon learns to recognize the "catastrophic reaction" (Goldstein¹²) — the gesture of failure by sudden abandonment of co-operation on the part of the patient. This requires patient and firm encouragement, the right mixture of sympathetic understanding and unyielding pressure, which is the most difficult yet essential feature of psychotherapeutic management to teach the younger medical officers. Its successful accomplishment springs from correct appraisal of the causes of breakdown.

The most valuable single factor in the management of head injury is undoubtedly that which might be called prophylactic psychotherapy. This is the affair of the ordinary physician or medical officer. Optimism is often said to be the essence of psychotherapy. Whereas this is surely true of nervous conditions in general, its wholesale application to head injuries is nearly as detrimental as undue pessimism. There is nothing more infuriating and discouraging than to be expected to achieve what is not possible. The successful management of head injuries therefore requires knowledge of what might reasonably be expected of the patient. To get a moderately severe head case up in the third week after injury brings the same troublesome sequelae as keeping a very mild case lying flat for four weeks. The first is discouraged by failure and takes a long time to get over the reaction; the second is convinced that some vital damage has occurred and will be anxiously on the *qui vive* for catastrophe for a long time afterward. The nature of the man and the severity of the injury must be taken into account. Insomnia and anxiety indicate underlying emotional tension. Regular discussion of difficulties, reassurance and encouragement to further performance are the keynotes of success. They are not time consuming, and the right kind of discussion for five minutes each day can accomplish more in the early stages than whole days of psychotherapy can correct at a later date. One of the commonest causes of relapse is the at-

itude taken by relatives, the family doctor or the medical officer of a convalescent home. Time and again, a patient who has progressed favorably has been allowed home to convalesce, and the first time he has had a mild headache has been taken by anxious relatives to the family doctor, who, hearing that he has had a head injury, insists on complete and prolonged rest in bed (instead of planned activity and less excitement). This strong suggestion is too much for many patients, who relapse forthwith. For this reason, a brief spell of active duty before a leave of absence is usually advised.

CONCLUSIONS

In conclusion, it is emphasized that the peculiar mixture of trauma and emotional shock that constitutes all war (and most civil) head injuries retains traces of both features throughout the convalescent period. Too frequently, emphasis is laid wholly on either structural damage or psychoneurotic state, with consequent failure to achieve the best results from treatment of both. Although particularly evident to the trained neurologist by reason of his familiarity with both functional and organic nervous disorders, the proportions of the mixture should be evident to anyone who takes time to sum up the pretraumatic nervous constitution and personality, the severity of the general brain injury, the residual intellectual and physical state, and the nature and degree of persistent anxiety. It is from lack of full appreciation of such factors that disappointment in the results of treatment arises. It is maintained that intensive effort along these lines not only will conserve and rapidly restore to duty officers and men the services can ill afford to lose but also will substantially reduce the great bulk of persistent disability that became a national calamity after at least one previous war.

The diagnostic and prognostic limitations of abnormalities in air encephalograms and electroencephalograms are discussed, and the important conclusion reached that some persistent defects in these are compatible with recovery without any disability. It is maintained that the key to most organic disability is defective intellectual function.

No single test will alone demonstrate a hopeless prognosis.

I am greatly indebted to my commanding officer, Lieutenant Colonel G O Chambers, M C, R A M C, for the privilege of making these comments and to Air Commodore C P Symonds, R A F V R, whose unfailing energy and advice was the inspring of the project, both in its inception and throughout its development. Finally, I should like to mention my associates, Majors W R Russell, W Reynell and M McArdle, of the R A M C, and the group of junior officers, without whose devotion, patience and care, especially in intelligence testing, the results that were achieved would not have been possible.

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MYELOID METAPLASIA OF THE SPLEEN WITH ACUTE HEMOLYTIC ANEMIA*

Report of a Case

LIEUTENANT HENRY H. BREWSTER, M.C., A.U.S.,† AND CAPTAIN O. J. WOLLENMAN, JR., M.C., A.U.S.‡

BOSTON

MYELOID metaplasia is a term applied to the formation of red blood cells, leukocytes and platelets in tissue in which they are not normally formed in extrauterine life.¹ Myeloid metaplasia of the spleen occurs to a minimal degree in a variety of diseases,² and to a maximal degree in myelogenous leukemia. Jackson, Parker and Lemon³ have recently reported 10 cases showing no evidence of leukemia, in which this abnormal process assumed, however, a major role. In their cases, the pathologic picture of the spleen and bone marrow differed sharply from that of leukemia and the response to radiation of the spleen was unfavorable. Clinically, several cases simulated acquired hemolytic jaundice. Hickling² had earlier observed evidence of blood destruction in 2 of 7 cases having what he called "chronic nonleukemic myelosis." Vaughan and Harrison,⁴ as well as Jackson et al.,³ found that the red-cell fragility was often increased. The case reported here represents one of fulminating hemolytic anemia in which the spleen, removed at operation, showed myeloid metaplasia. It was possible to investigate the nature of the hemolytic process and to obtain evidence why removal or radiation of such a spleen has been found^{2, 3} to be a dangerous procedure.

CASE REPORT

M. L. (B. C. H. 1002063), a 25-year-old, white, American housewife, was referred to the Boston City Hospital on October 21, 1940. Except for icterus neonatorum, which cleared within the 1st week of life, and swollen left-cervical lymph nodes removed in infancy, she had always enjoyed robust health. During the year prior to entry, she had tired easily and grown increasingly pale. On September 2, 1940, she experienced severe occipital pain and felt drowsy. She grew progressively weaker the next day and passed a specimen of red urine. On September 4, her temperature was 102°F. Believing that she had pyelitis, a physician gave her 40 gr. of sulfanilamide in the course of 2 days, after which she became confused. On September 6, she was admitted to a local hospital, where on examination she appeared drowsy, pale and slightly icteric. Edema of the ankles and face was present. The temperature was 102°F. A soft systolic murmur was heard over the pulmonic area. On admission, the red-cell count was

1,000,000, the white-cell count 18,000, and the hemoglobin 25 per cent (Sahli—3.9 gm. per 100 cc.). Albuminuria was found repeatedly. X-ray films of the chest demonstrated mottled clouding extending 6 cm. from the hilus toward the periphery of each lung. During her 3 weeks in that hospital, the patient received twenty-two

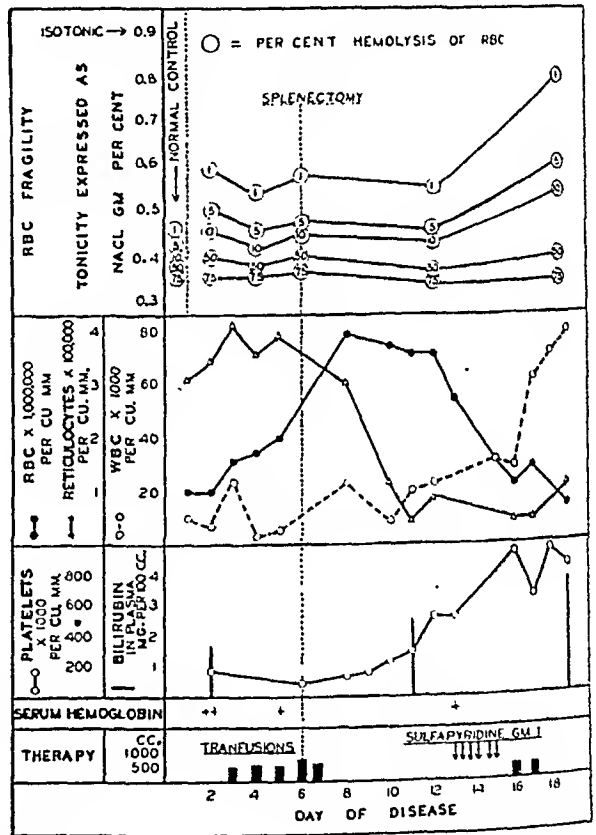


FIGURE 1. Blood Findings in a Case of Acute Hemolytic Anemia with Myeloid Metaplasia of the Spleen.

The red-cell-fragility determinations were performed on blood from an antecubital vein on the first, fourth and twelfth days, from the splenic vein on the sixth day and from the radial artery on the eighteenth day. The meaning of the "R.B.C. fragility" curve is as follows: (1) on the eighteenth day means that 1 per cent of the patient's red cells hemolyzed in 0.80 per cent salt solution in comparison with 1 per cent of those of a normal person in 0.46 per cent salt solution.

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) and the Mallory Institute of Pathology, Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston.

†Formerly, research fellow in medicine, Harvard Medical School, and assistant resident physician, Thorndike Memorial Laboratory, Boston City Hospital.

‡Formerly, assistant in pathology, Mallory Institute of Pathology, Boston City Hospital.

transfusions as well as parenteral liver extract, Vi-Penta and Feosol tablets and Mead's brewer's yeast. In spite of this treatment, the red-cell count remained about 1,000,000. Both the spleen and liver became palpable. The temperature, edema and icterus subsided practically to normal.

The patient was transferred to this hospital 7 weeks after the onset of fever and extreme weakness. On examination, she appeared pale, sallow and drowsy, she was scarcely able to move in bed. Her temperature was 102.5°F, the pulse 126, the respirations 18, and the blood pressure 102/40. No petechiae, purpura or telangiectases were found, although flame-shaped hemorrhages were observed in the fundus of the right eye. The lungs were clear. The heart was of normal size, a soft systolic murmur was heard over the pulmonic area. The spleen descended 5 cm below the costal border on inspiration and extended medially to the midclavicular line. The liver edge was palpable at the costal border. The abdomen was tense and distended but not tender. There was slight edema of both ankles. No clubbing of the extremities or enlargement of lymph nodes was present. Examination of the pelvis, rectum and nervous system revealed no abnormality.

Of chief interest were the blood changes, shown in Figure 1. The initial white cell count was 10,100, with 61.5 per cent neutrophils, 13.5 per cent band forms, 0.5 per cent eosinophils, 1.0 per cent basophils, 5.0 per cent small lymphocytes, 6.5 per cent large lymphocytes, 6.5 per cent monocytes, 0.5 per cent young monocytes, 1.0 per cent myelocytes and 4.0 per cent metamyelocytes. The hemoglobin was 23 per cent (Sahli—36 gm per 100 cc.). The red-cell count was 1,000,000, with 31 per cent reticulocytes. In addition, there were 55 nucleated red cells per 1000 white cells. The red cells varied greatly in size but little in shape, the majority being macrocytes, there were no fragmented cells. The hematocrit reading was 12.2 per cent, the mean corpuscular volume 122 cubic microns, and the mean corpuscular hemoglobin concentration 29.4 per cent. A wet preparation of red cells showed no evidence of sickling in 24 hours. The fragility of the red cells in hypotonic salt solutions was significantly increased.

The plasma bilirubin was increased to 1.73 mg per 100 cc. (normal, 0.2 to 0.7 mg)⁵. The serum contained 60 mg of free hemoglobin per 100 cc (normal, trace to 50)⁶. The plasma protein amounted to 5.5 gm per 100 cc. albumin 2.89 gm, globulin 2.36 gm and fibrin 2.49 mg. The blood nonprotein nitrogen ranged between 26 mg per 100 cc on the 1st day and 29 mg on the 16th day. The icteric index varied from 15 to 25 units. On the 1st and 12th days, the Donath-Landsteiner Test,⁷ the hemolysis test with acidified serum⁸ and the test for autohemolysis⁹ were all negative. Autoagglutinins were insignificant, being present in only a 1:8 dilution at 0°C.⁹

Repeated specimens of urine were acid, had a specific gravity varying from 1.022 to 1.012, showed a + test for albumin and contained many white cells, but no red cells, bile or hemoglobin. A culture was positive for *Escherichia coli*. From a portion of a 24 hour sample, the urobilinogen excretion was estimated to be 5 mg per 100 cc.¹⁰ Bile was present in the stools, occult blood was absent.

In the first 5 hospital days, the patient received four transfusions, each averaging 600 cc of blood. On the 6th day, the spleen was removed. Red cells obtained from the splenic vein blood at operation were just as fragile as those previously tested (Fig 1). With the aid of transfusions, the red-cell count rose to 4,000,000 following the operation, but within 6 days fell to 700,000. The nucleated red cells rose from 55 to 175 per 1000 white cells, while reticulocytes fell from 30.8 to 4.4 per cent (43,800 per cubic millimeter). The white cell count increased from

10,000 to 79,000, with 1 per cent myeloblasts. The platelet count, originally 200,000, reached 900,000. The plasma bilirubin rose from 1.7 to 3.7 mg per 100 cc, and free hemoglobin persisted in the serum, although in lesser amounts. The fragility of the red cells in hypotonic salt solution increased still further.

The patient received three blood transfusions following operation, but even these failed to check the progressive anemia. On the 12th hospital day, x-ray films of the chest, which were normal on admission, demonstrated infiltration of the right supraclavicular region and fluid at the right base. No organisms grew out of a blood culture taken on the tenth day. She received 90 gr of sulfapyridine in divided doses by mouth on the 13th and 14th days. Because of the excessive nausea and vomiting that ensued and because of a falling red-cell count, this medication was discontinued. The temperature continued to spike to 103°F, and edema appeared in the legs. The patient died on the 19th hospital day.

The spleen, removed at operation, weighed 710 gm. Its capsule was smooth, its consistence firm. On section, the cut surface was dark red gray with several scattered yellow soft areas varying from 0.6 to 4.0 cm in diameter. Neither the Malpighian corpuscles nor the trabeculae were prominent. Scanty blood scrapings were obtained from the surface. The splenic artery and vein were not remarkable. On microscopic examination, the Malpighian corpuscles were found to be fairly well preserved. Fibrosis of the pulp was diffuse and moderately extensive. Numerous clumps of myelocytes with rare adult granulocytes were prominent. Many foci of red cell formation were present. Megakaryocytes were moderately numerous throughout the section. Many of the macrophages seen contained hemosiderin. The histologic picture was typical of myeloid metaplasia, and in no way suggestive of that seen in hemolytic jaundice.¹¹

Autopsy (A40914). The body was examined 3 hours post mortem. Type 3 pneumococcal lobar pneumonia was found, as well as a recent infarct of the right upper lobe of the lung. The infarction was embolic from an ante-mortem blood clot of the right femoral and saphenous veins. There were icterus, pallor, pulmonary edema, peripheral edema, bilateral hydrothorax, hydropneumothorax, hepatomegaly (1810 gm) and hyperplasia of the vertebral, sternal, costal and femoral marrows. The tibial marrow was composed entirely of fat.

Microscopically, the liver and kidneys showed an abundance of hemosiderin but no evidence of myeloid metaplasia. A small degree of myeloid metaplasia was present in the scar tissue at the site of splenectomy and in one cervical lymph node. The vertebral, sternal, costal and femoral bone marrows were hyperplastic in both the red cell and white cell series. The usual number of megakaryocytes was found. Hyperplasia of the red cell series only slightly exceeded that of the white-cell series. Many immature forms of both series were observed, although normally matured cells were by no means absent.

DISCUSSION

Excessive hemolysis of red blood cells occurred in this patient, as evident from the severe and persistent anemia, hemoglobinemia and bilirubinemia in the absence of bilirubinuria. The pathogenesis of this hemolysis was sought among the known causes of hemolytic anemia.

First, a search was made for hemolysins. Tests for Donath-Landsteiner hemolysin⁷ and autohemolysin⁸ were negative. Hemolysin arising from the spleen⁸ was excluded by the fact that the signs of hemolytic anemia persisted after splenectomy. There was no evidence of transfusion reactions or of an infection by such hemolytic organisms as the hemolytic streptococcus or *Clostridium welchii*.¹² Secondly, agglutinins were looked for, because hemagglutination can, as Ham and Castle¹³ have demonstrated, produce hemolytic anemia. Tests for autoagglutinins⁹ were negative. No unusual isoagglutination was observed when the patient's blood was cross-matched with those of the donors.¹⁴

A third cause of hemolytic anemia is an abnormality of the erythrocytes. The origin may be extrinsic, as in malaria and Oroya fever, or intrinsic to the erythrocytes, as in paroxysmal nocturnal hemoglobinuria. That the patient's red cells did not hemolyze in acidified serum of the same blood group excludes the last diagnosis.⁶ Failure of the red cells to sickle eliminated the possibility of sickle-cell anemia; however, the morphology of the erythrocytes was suggestive of Cooley's anemia.¹² This diagnosis was not tenable because the patient was not of Italian stock, because her family gave no history of anemia, but chiefly because her red cells were more fragile than normal. Finally, examination of blood smears disclosed no organisms to suggest the diagnosis of malaria or Oroya fever.⁹

The next cause of hemolysis considered was some noxious agent. The patient could recall no exposure to the fava bean¹⁵ or lead.¹² On the other hand, the family stated that the patient had used much Energine, which contains carbon tetrachloride, to clean her shoes. Furthermore, her husband used to make model airplanes in the bedroom and employed a glue that probably had a benzene base. At the commencement of her illness, the patient received 40 gr. of sulfanilamide. It is unusual, however, for sulfanilamide¹⁶ to cause a hemolytic anemia that persists despite transfusions for two months following withdrawal of the drug. The effect of sulfapyridine given to the patient on the thirteenth hospital day is more difficult to appraise. That extreme hemolysis occurred in the five days after sulfapyridine therapy is evident from the decrease in the red-cell count from 2,500,000 to 700,000. But this rate of destruction is comparable with the drop from 4,000,000 to 2,500,000 during the two days preceding sulfapyridine therapy. Therefore, sulfapyridine cannot be considered a significant hemolytic agent in this case.¹⁷

There was an extreme increase in the fragility of the red cells. Congenital hemolytic jaundice was excluded by demonstrating that both parents had completely normal blood values. The cause of the abnormal fragility in this patient cannot be stated, although it is clear from the recent work of Ham and Castle¹³ that increased fragility of erythrocytes predisposes to an abnormal degree of hemolysis. To recapitulate, the increased fragility of red cells was the only evidence found in this patient for an abnormal mechanism of their destruction.

What role did the spleen play in this hemolytic anemia? Except for the finding of myeloid metaplasia of the spleen,* the anemia had the characteristics of acute hemolytic anemia: vigorous erythropoiesis, as indicated by high concentrations of reticulocytes before operation; excessive hemolysis, evident from anemia; hemoglobinemia; and bilirubinemia. Because splenectomy did not diminish the already increased fragility, the spleen was clearly not the cause of it. On the other hand, the failure of the reticulocytes to increase after splenectomy as the anemia progressed suggests that the spleen, before its removal, was an important organ of erythropoiesis. The low postoperative reticulocyte count might be interpreted as a sign of toxic inhibition of red-cell production by sulfapyridine. Against this interpretation stand the observations that sulfapyridine does not inhibit reticulocytosis and that when a hemolytic anemia is produced by sulfapyridine therapy,¹⁸ inhibition of white-cell and platelet production, often associated with toxic anemias, did not occur. Hence, the post-splenectomy disappearance of reticulocyte response probably means that the removal of the spleen deprived the patient of an important erythropoietic organ—a conclusion consistent with the experience of other investigators.^{2, 3}

SUMMARY

A case is reported of acute hemolytic anemia with myeloid metaplasia of the spleen, in which splenectomy was performed.

Increased erythrocyte fragility was the only evidence found of an abnormal mechanism of destruction of red blood cells. The cause of this increased fragility was not discovered. Splenectomy did not cause decrease in the fragility.

The disappearance of signs of blood production subsequent to splenectomy indicates that the spleen was, in this case, an important blood-forming organ, the removal of which probably reduced the erythropoietic capacity of the body resulting in a fatal anemia.

*Dameshek and Schwartz⁵ found myeloid activity in an impression smear of the spleen of acute hemolytic anemia, but they did not record the pathologic findings in this organ.

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DURAL CONSTRICTING RING WITH CERVICAL PROTRUDED INTERVERTEBRAL DISK

Report of a Case

CAPTAIN WALTER G. HAYNES, M.C., A.U.S.*

THE incidence of the Arnold-Chiari malformation at the foramen magnum, associated with syringomyelia or hydromyelia of the upper cervical cord, has been noted by a number of authors, notably Gustafson and Oldberg,¹ D'Errico,² Russell and Donald,³ Rosenblath⁴ and Lichtenstein.⁵ All these authors mentioned the occurrence of syringomyelic cavities in association with the true Arnold-Chiari malformation. Lubin⁶ thought that chronic adhesive spinal arachnoiditis might cause intramedullary cavitation. Mackay⁷ reported a case of cervical arachnoiditis with cavitation and implied a causative effect. Schwarz⁸ believed that syphilitic pachymeningitis cervicalis also could cause cavitation. Gustafson and Oldberg mentioned the incidence of the syringomyelic cavity associated only with a dural constricting ring which was, in their cases, accompanied by a deformity of the foramen magnum.

Although there were no positive statements by any of the authors mentioned to the effect that this foramen magnum deformity or the dural constricting ring contributed to the formation of the cyst, the general implication throughout their articles was that a dural ring constricting the cord at the level of the foramen might have contributed to the formation of the cyst. It was further intimated that this could be caused by interference with the vertebral artery at the foramen or interference with the circulation of cerebrospinal fluid through the foramina of Magendie and Luschka,

thus causing either hydromyelia or hydrocephalus or both. These conditions would be more apt to be caused by the complete Arnold-Chiari malformation, with a herniation of the cerebellar tonsils to occlude completely or partially the fluid passageway. Hassin,⁹ however, spoke of the prevalence of arachnoid and dural reaction at the level of and above the syringomyelic cyst, and this condition he considered to be secondary to the syringomyelic cavity rather than a causative factor. This view is also borne out by Schlesinger,¹⁰ who reported the occasional findings of dural and arachnoid adhesions at the level of or above the cyst. Hassin¹¹ maintained, furthermore, that the fact that meningeal changes in syringomyelia are not always mentioned or emphasized by authors indicates that they cannot be a primary factor, since, if such changes do not exist, they cannot produce a cavity or any other process in a spinal cord. On the contrary, he believed that a long-standing or advanced syringomyelic cavity or other space-occupying lesion of the cervical cord might cause meningeal changes.

This latter view is favored by the following report of a patient in whose case the space-occupying lesion at the level of the fifth cervical vertebra was not a syringomyelic cyst but a protruded intervertebral disk. This disk was accompanied by an arachnoid reaction, which surrounded it, extended upward and culminated in severe arachnoid proliferation, dural thickening and the formation of a dural constricting ring at the level of the foramen magnum. Complete roentgenographic studies re-

*Chief of the Neurosurgical Section, Lovell General Hospital, Fort Devens, Massachusetts.

vealed no evidence of platybasia or upper cervical malformation, and none was found at the time of operation. It must be emphasized that this was not a case of true Arnold-Chiari malformation, and no argument is advanced in this report to the effect that a space-occupying lesion could cause an Arnold-Chiari malformation.

CASE REPORT

A 36-year-old man entered the Lovell General Hospital on October 24, 1941. His complaints at that time were confined to soreness in the right arm, which he had first experienced 2 months prior to admission. The pain had been persistent, but was worse at some times than others, particularly when the weather was damp or cold. It had progressed to involve the entire upper extremity and radiated from the back down the arm along the ulnar side. The pain was usually dull and aching but was interspersed with many sharp, shooting pains which were made worse by coughing or sneezing. At another hospital, roentgenograms revealed a dislocation of the 5th cervical vertebra on the 6th. The patient was placed in traction, but since this made his pain worse, it was discontinued.

On admission, no history of injury to or about the vertebral column could be elicited. There was a long-standing history of loss of weight, cough and so forth, suggesting tuberculosis. There was also a history of prostatitis.

Physical examination revealed a thin, emaciated white man, but was otherwise negative. Neurologic examination of the cranial nerves was negative, except for a fine, sustained nystagmus on looking to the left. There was a slight loss of power of the right arm and leg. There was no anesthesia or hypesthesia. There was some tenderness on percussion of the 4th cervical vertebra. All the reflexes on the right side were markedly increased over those on the left side, with a sustained ankle and patellar clonus and positive Hoffmann, Chaddock and Rossolimo signs on the right. The cremasteric reflex was absent on the right, as were both abdominal reflexes. Roentgenograms taken in all positions were negative, and the previous report of a dislocation of the 5th cervical vertebra on the 6th could not be verified. Spinal puncture revealed evidence of an almost complete subarachnoid block, with an increased spinal-fluid protein and a positive Pandy reaction. Fluoroscopic examination of the chest revealed an old, healed cavitation in the apex of the right lung, which was interpreted to mean an old, healed tuberculosis. A prostatic smear revealed a few pus cells. The remainder of the study was entirely negative.

A diagnosis was made of either cervical arachnoiditis or a cervical protruded intervertebral disk at the 5th and 6th cervical vertebrae. A laminectomy was performed November 21, 1941. The operative note was as follows:

Under endotracheal ether, the usual subperiosteal exposure of the laminae of the 3rd, 4th, 5th and 6th cervical vertebrae was carried out. This exposure was unduly difficult because of increased vascularity; however, with the help of the Bovie unit, this was controlled until it became necessary to remove the spines and the laminae. A large plexus of dilated veins was found between the dura and each lamina, and every time a portion of the bone was removed, this plexus was torn, causing furious bleeding, which was checked with difficulty. Eventually, however, the dura was exposed under the laminae of the 3rd, 4th and 5th

cervical vertebrae. The dura was opened and there was immediately a large gush of yellow cerebrospinal fluid. This opening was extended, and a mass of arachnoid adhesions, which were diffuse and fine, was exposed. At the caudal end of the incision a bulging of the cord could be seen. The cord appeared large and flattened in this area, so that a syringomyelic cyst was suspected. The hypodermic needle was inserted between the posterior columns, and the area aspirated; but no cystic material could be obtained. The incision was therefore extended caudad to expose and remove the bone and to open the dura over the defect. It could then be seen that the bulge in the cord was not due to a cyst, but rather to a space-occupying lesion beneath the cord, which pushed it posteriorly. On gentle retraction of the cord by means of the dentate ligament, a fairly large herniated intervertebral disk was discovered at the interspace between the 5th and 6th cervical vertebrae, lying on the right side of the cord and compressing the roots emanating from the cord. This protrusion measured approximately 2 cm. and extended across the intervertebral-disk space almost to the other side. The ligamentum flavum was trimmed away and this area was decompressed. A catheter was then passed with ease over the obstruction. On attempting to pass a small catheter cephalad, however, another obstruction was met under the first cervical vertebra, so that the incision was then extended in this direction and the dura opened. Here was found a marked thickening of the dura and arachnoid with an actual constricting ring compressing the cord and causing a complete block in this area, just below the foramen magnum. No bone deformity could be found, although the foramen magnum was inspected thoroughly. This area was decompressed so far as possible, and the dura was left open so that a catheter could be passed with ease in this direction. Hemostasis was obtained with difficulty, and the wound was closed in the usual fashion. The condition of the patient at the termination of the operation was good.

Diagnosis: Protruded intervertebral disk at the 5th and 6th cervical vertebrae, with a dural and arachnoid proliferation to form a constricting ring at the foramen magnum.

The postoperative course was satisfactory until 2 months later, when the patient complained of a reddened, tender area in the incision line. This was opened and found to contain pus. Accordingly, the entire area was opened, cleaned out and allowed to granulate in from the bottom. This was accomplished without difficulty. The patient still exhibited pyramidal tract signs, which gradually disappeared. Five months later, he walked without a limp and had no pain, but still exhibited positive Rossolimo and Hoffmann signs on the right. There was no limitation of motion in the neck.

SUMMARY AND CONCLUSIONS

A case is reported in which a severe arachnoid and dural reaction at the foramen magnum was interpreted as being secondary to a cervical-cord space-occupying lesion, in this case a protruded intervertebral disk.

In the absence of platybasia or other bony deformity, a dural and arachnoid constricting ring

was found at the level of the foramen magnum, the reaction apparently starting at the level of the protruded intervertebral disk at the fifth cervical vertebra and extending cephalad, becoming very marked at the foramen.

It is suggested that, contrary to general opinion, the syringomyelic cavity below a dural constricting ring at the foramen magnum is not secondary to the malformation, but causes the dural and arachnoid reaction resulting in the malformation.

This report does not attempt to explain the syringomyelic cavity found in the cases of platybasia where the odontoid process has caused a dural reaction resulting in the same constricting ring

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THE DIAGNOSTIC VALUE OF SERIAL MEASUREMENTS OF ALBUMINURIA IN AMBULATORY PATIENTS*

HARRY A. DEROW, MD†

BOSTON

UNSUSPECTED albuminuria is frequently found in apparently healthy individuals. It is often difficult to decide whether or not this finding is indicative of organic renal disease. Many authors have attempted to evaluate the significance of such apparently incidental albuminuria.¹⁻⁶ Studies in ambulatory patients with albuminuria of the concentration of albumin in consecutive samples of urine voided over a period of twenty-eight to thirty-four hours have yielded information of help in the differentiation of benign from pathologic albuminuria. The present report analyzes the findings in such cases, the studies will be continued for many years, additional data being obtained on these patients as well as on all similar ones who come to our notice.

MATERIALS AND METHODS

Three hundred and fifty-nine studies were made on 123 ambulatory patients. Twenty-six of these patients had other signs and symptoms establishing the diagnosis of glomerulonephritis. Eight patients had pyelonephritis, 2 had lupus erythematosus, and 42 had primary arterial hypertension. In 45 patients none of the above diagnoses were made, patients with congestive heart failure, diabetes mellitus or certain diseases of the genitourinary tract were not included in this group.

The following printed form was given to each patient before the start of each study.

*From the Nephrology Clinic and Medical Service, Beth Israel Hospital and the Department of Medicine, Harvard Medical School.

†Instructor in medicine, Harvard Medical School, associate visiting physician, Beth Israel Hospital.

Albuminuria Test

Before starting this test, secure 6 to 10 clean, dry 4-ounce bottles. Female patients should use clean, dry, wide-mouthed jars.

Paste a blank label on each bottle. Number each bottle consecutively beginning with 1. Write the hour and date of voiding on the label as each bottle is consecutively used.

1. One hour after going to bed at night, empty your bladder *while still in bed*, using a bed pan or bottle, have someone else discard this urine.

2. When you awaken in the morning, *while still in bed*, pass your urine into bottle No. 1.

3. Get out of bed, and kneel on the floor with your head erect and your shoulders thrown back for 10 minutes by the clock. Then, *while still kneeling*, pass your urine at the end of this time into bottle No. 2.

4. Do not drink any liquids (water, coffee, tea, soups, milk and so forth) all day.

5. You may now have your breakfast and go about your daily routine.

6. From now on, whenever you have to pass your urine, do so into one of the labeled bottles or jars, and write the date and hour of voiding on the label.

7. The last urine saved will be that which is passed in the morning.

8. Please bring all the bottles, properly labeled to the clinic (or office) on the morning.

Each sample of urine was tested for albumin by the Heller ring method, as follows: Approximately 2 cc of concentrated nitric acid was poured into a small wineglass, and the urine was filtered so that the filtrate overlies the acid. After an interval of one minute, the line of contact of the urine and acid was carefully observed for the

presence of a white ring indicating the presence of albumin. A ring seen only against a black background was considered a slightest possible trace (<+); a ring observed against any background was considered a very slight trace (+); a ring seen against any background and just visible from above was considered a slight trace (++); a ring which was opaque from above was considered a trace (+++); and a very flocculent ring opaque from above was considered a large trace (++++).

In the performance of the Heller ring test for albumin, it is important to use clean glassware, good filter paper (Whatman's No. 1) and a good light source. Cloudy and alkaline urines should be centrifuged before they are filtered.

The specific gravity and reaction to litmus of each sample of urine were also determined. The sediment obtained by centrifuging the sample passed in the clinic or office was studied for formed elements.

RESULTS

Constant albuminuria. In 62 patients (Table 1), albumin was present in *all* samples of urine, irrespective of the time of day, activity or position. The lordotic position usually had no effect on the albumin excretion, while the assumption of an upright position usually resulted in an increase in excretion of albumin over that of the recumbent position.

Postural albuminuria. In 40 patients (Table 1), albumin was not found in the morning sample

the end of the ten-minute period of exaggerated lordosis. Albuminuria continued throughout the day until evening.

Type 3. Albumin was not found in the urine voided at the end of recumbency and after lordosis.

TABLE 2. Time of Occurrence of Albuminuria in Ambulatory Patients.

KIND OF ALBUMINURIA	AFTER NOCTURNAL RECUMBENCY	AFTER TEN-MINUTE LORDOSIS	AMBULATORY STATE			
			MORNING	NOON	AFTER NOON	EVENING
None	0	0	0	0	0	0
Constant	+	+	+	+	+	+
Postural						
Type 1	0	+	+	0	0	0
Type 2	0	+	+	+	+	0
Type 3	0	0	+	+	0	0
Type 4	0	0	+	+	+	0
Type 5	0	0	0	0	+	+

+ = albumin present, 0 = albumin absent

dosis. It appeared promptly after the upright position was assumed and continued until midday, but was absent in the afternoon and evening.

Type 4. Albumin was not present in the urine voided during recumbency and after lordosis, but appeared in the urine voided after the upright position was assumed; it continued to appear until evening.

Type 5. Albumin was present in the urine only in the afternoon and evening.

Types 2 and 5 of postural albuminuria were most frequently found. The type usually varied

TABLE 1. Clinical Diagnoses and Types of Albuminuria.

DIAGNOSIS	CONSTANT ALBUMINURIA		POSTURAL ALBUMINURIA		OCCASIONAL ALBUMINURIA	
	NO. OF CASES	NO. OF STUDIES	NO. OF CASES	NO. OF STUDIES	NO. OF CASES	NO. OF STUDIES
Overt chronic glomerulonephritis	22	64				
Overt chronic pyelonephritis	6	28				
Overt healing acute glomerulonephritis			4	14		
Overt healing acute pyelonephritis			2	6		
Lupus erythematosus	2	7				
Primary arterial hypertension	21	52			21	62
No diagnosable renal disease	11	32	34	94		
Totals	62	183	40	114	21	62

of urine collected in bed. Albuminuria appeared following the assumption of the upright position and activity. The findings in this group (Table 2) fell into five categories:

Type 1. Albumin was not found in the urine collected at the conclusion of the period of recumbency; there was marked albuminuria at the end of a ten-minute period of exaggerated lordosis. Albuminuria disappeared by midday.

Type 2. Albumin was not found in the urine collected at the conclusion of the period of recumbency; there was marked albuminuria at

from time to time in a given patient. Occasionally in a patient with postural albuminuria, albumin was absent from the urine during a given test period, only to recur in subsequent studies.

Occasional albuminuria. In 21 patients (Table 1), albumin was found in the urine occasionally without any relation to recumbency, lordosis, the upright position or activity.

COMMENT

The test. The purpose of the voiding one hour after going to bed was to eliminate the possibility

of including in the morning sample urine formed while the patient was up and about the day before. The conditions of a concentration test were observed during the entire day by the rigid restriction of the intake of fluid so that if the maximum specific gravity was 1.026 or higher in one of the samples, renal function was considered to be normal.

No matter what the etiology of the albuminuria is, the urine voided in the midmorning after the patient has been up and about will show albumin oftener than any other voided during the twenty-four hour period (Table 2). This fact must be borne in mind in studies of the incidence of albuminuria.

Constant albuminuria. The finding of albumin in all samples of urine, regardless of the time of day, position or activity, in the 30 patients with overt glomerulonephritis, pyelonephritis and lupus erythematosus is strong evidence that constant albuminuria indicates organic renal disease. In this group are included 7 patients with chronic latent glomerulonephritis who have been followed for five to ten years after the initial attack of the disease. These patients, although symptomless and nonhypertensive, have shown constant albuminuria with normal renal function. If the initial attacks had been insidious instead of overt, one might be at a loss to explain the constant albuminuria.

The finding of constant albuminuria in 21 patients with primary arterial hypertension is further evidence that constant albuminuria indicates some form of chronic disease involving the kidney. In patients with primary arterial hypertension albuminuria may be absent for many years, later it may appear in an occasional urine, to be followed after a period of months or years by constant albuminuria, but never by postural albuminuria.

Of the 11 patients with constant albuminuria with no definitely diagnosable renal disease when first seen, one subsequently developed the manifestations of an acute episode of glomerulonephritis, another developed those of an acute episode of pyelonephritis, and a third developed hypertension after albuminuria had been constant for a long period of time. It is therefore believed that constant incidental albuminuria as above defined, with or without hypertension, indicates organic renal disease.

Postural albuminuria. Six patients recovering from an initial attack of glomerulonephritis or pyelonephritis showed postural albuminuria for several months before the albuminuria completely disappeared. The appearance of postural albuminuria in such patients, therefore, should not be regarded as evidence of persistent renal disease.⁷

Postural albuminuria of one type or another maintained over a period of months or years was

found, however, in patients in whom the history, physical examination and study of the urinary sediment failed to reveal anything suggestive of organic renal disease. None of these patients developed either constant albuminuria or overt renal disease. The finding of persistent postural albuminuria is therefore not to be considered evidence of organic renal disease.

Occasional albuminuria. Occasional albuminuria was found in patients with many conditions.^{8,9} It is significant only in patients with primary arterial hypertension where it may be followed after a period of months or years by constant albuminuria.

CONCLUSIONS

A method of study of albuminuria in ambulatory patients without symptoms is presented. It consists of the study of the concentration of albumin in consecutive samples of urine voided over a period of twenty-eight to thirty-four hours under fixed test conditions.

Such albuminuria may be constant, postural or occasional.

Constant albuminuria is found in all patients with overt chronic nephritis.

Postural albuminuria is present in patients without any evidence of organic renal disease. A small number of patients recovering from an initial attack of overt nephritis show postural albuminuria for several months before the urine becomes free of albumin.

Constant albuminuria even in the absence of any history of an antecedent overt episode and of any other findings is indicative of organic renal disease.

Patients with primary arterial hypertension may show no albuminuria or may show occasional albuminuria or constant albuminuria, but never postural albuminuria.

The urine voided in the midmorning after the patient has been up and about will show albumin more often than any other voided during the twenty-four hour period.

520 Beacon Street

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MEDICAL PROGRESS

CANCER*

IRA T. NATHANSON, M.D.†

BOSTON

STATISTICS of the past decade reveal a decided increase of cancer in the general population. They also demonstrate that the rise will continue at a more rapid rate in the next quarter of a century unless more adequate preventive and specific measures are established. Advances in the prevention and therapy of other diseases are in part indirectly responsible for this rise in the cancer rate, inasmuch as they have significantly prolonged the life expectancy of the individual. It has been shown that the probability of the development of cancer increases steadily with advancing age.¹ It is obvious, therefore, that the cancer problem will become more important since it is the second cause of death in this country even at the present time. Recognition of these facts has led to a recent increase in interest in both the clinical and experimental aspects of the disease. This is evident from the accumulated literature on the subject and the establishment of public-health programs and new institutes and clinics. It has often been said that experiments on cancer in the laboratory animal cannot be applied to the problem in human beings. These statements are only partially true; for evidence will be presented which suggests that utilization of observations in both the human being and the animal is necessary to study more intimately the nature of the disease. There are many analogies in cancer between man and beast.

It is the purpose of this review to present the more practical and interesting aspects of the problem, in the hope, that they may stimulate the physician to a more careful search for preventive, diagnostic and therapeutic procedures, and to inform him of the possibilities of advance in the future.

ETIOLOGIC FACTORS

Precancerous Lesions

Much of the recent work has been centered around precancerous lesions. Recognition of such tissue change is obviously of the greatest importance, since effective treatment would do much to

lessen the incidence of cancer. Precancerous tissue is that which has a greater tendency to develop cancer than other tissue. It has been recognized more and more that neoplastic disease seldom develops in healthy structures. The theory of chronic irritation is compatible with this viewpoint. Distortion of healthy tissue by trauma or by disease appears to be in the same category. Moreover, it is known that atrophic and degenerative changes appear with old age. It was pointed out above that the liability to cancer increases with old age, suggesting that most individuals may develop the disease. Is this a result of changes in cellular metabolism that render the organism susceptible to a potential carcinogenic factor? At any rate, it is apparent that the substrate or soil is a most important factor in determining the effect of an unknown agent in the production of cancer. Factual data suggest that these factors are closely interwoven.

Rhoads² has summarized known precancerous lesions as follows:

Skin

- Keratoses of atrophic skin
- Xeroderma pigmentosa (atrophy)
- Radiation dermatitis (atrophy)
- Burn scars and lupus (atrophy)
- Arsenic dermatitis (atrophy)

- Kraurosis vulvae (atrophy)
- Plummer-Vinson disease (atrophy)
- Thyroid cancer after hypothyroidism
- Cancer in undescended atrophic testicle
- Cancer of liver on cirrhosis
- Leukemia on aplastic anemia

To these may be added suspected and other known precancerous lesions such as those from hormonal and vitamin deficiencies, leukoplakia, chronic gastritis, chronic mastitis, Paget's disease of the bone, luetic glossitis, and changes produced by chemical, thermal, actinic and physical injury that frequently precede or accompany the development of carcinoma.

Pack and Wuester³ in discussing the onset of cancer of the skin point out that this process "is initiated by two factors at work; one an intrinsic change in the structure and function of the skin whereby it loses in some degree its protective capacity against injuries, and the other an extrinsic

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, Vol. III, 1942* (Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

*This is publication Number 561 of the Cancer Commission of Harvard University.

†Instructor in surgery, Harvard Medical School; assistant in surgery, Massachusetts General Hospital; assistant surgeon, Pondville Hospital.

factor such as mechanical trauma or physical irritation." It is held that the majority of cancers of the skin and stratified mucous membrane may be "scar" cancer.^{3, 4} Many of these lesions on which cancer originated may have been so small as to pass unnoticed, or may be obscured by the cancer itself. Similar changes may precede cancer in other organs that are not available for direct examination.

Diet

At periodic intervals statements have appeared by scientific workers, and quacks as well, that certain diets or elements in the diet are conducive to the formation of cancer. These ideas have been discarded as frequently as they appeared because of lack of confirmatory data. However, in recent years observations have been made in human subjects and laboratory animals that suggest a possible etiologic relation between cancer and diet.

It has been demonstrated that variations of the diet in mice can significantly alter the incidence of several types of spontaneous and induced tumors.^{5, 6} Mice that remained healthy on a calorie-restricted diet but containing the essential dietary elements showed a lesser incidence of tumor formation as compared with the controls fed *ad libitum*. Moreover, the addition of fat to the basal ration to render the diet high in calories significantly increased the incidence of certain tumors, whereas others were unaffected.⁷⁻⁹ It may be concluded from these studies that the alteration of the caloric content alone was responsible for the results obtained, although other factors may be involved as a result of the additional fat. The application of these experimental studies to human cancer may prove significant. A review of life-insurance statistics dealing with the relation of body weight to cancer reveals that overweight persons are likelier to develop cancer than those who are average or underweight.¹⁰

However, other factors in the diet may be of importance. One of the most fascinating studies is that of primary cancer of the liver. It has been observed that the disease is common among all pigmented races, in some instances over forty times as frequent as in Whites. The Japaoese, the Javanese, African aborigines and the Chinese have the highest incidence. Filipinos and British Indians are also peculiarly susceptible.¹¹ Racial factors may play a prominent role; on the other hand, the radically different dietary and drinking habits of these races may be of equal or greater importance, especially since cirrhosis of the liver is almost always associated with the cancer. It is likely that both factors operate in the production of the disease.

Many attempts have been made to prove the influence of diet on cancer production. Kinosita,¹² using dimethyl-amino-azobenzene, known as butter yellow, was successful in producing liver cancer in rats. It is interesting that, as in human beings, certain strains of rats developed the hepatoma more readily than others. In most cases the cancer was preceded by cirrhosis. The basic diet used was rice, to simulate the food of the natives. It was further found that substitution of wheat bread for rice markedly reduced the incidence of the cancer.¹³ Following these observations much has been done to find other agents that might be effective in the production and inhibition of the disease. For example, feeding of furfural, which is an ingredient of the Japanese rice wine, sake, to rats resulted in liver cirrhosis but no cancer.¹⁴ Edwards¹⁵ fed carbon tetrachloride to mice and produced hepatomas in 100 per cent of the cases.

It is now known that the addition of yeast, rice-bran extract, yeast extract, liver and kidney reduces the incidence of butter-yellow-induced liver cancer. Diets supplemented by riboflavin and casein, or with combinations of the members of the vitamin B complex, alone or in addition to cystine and choline, are also effective in prevention of the hepatoma.¹⁶ Of further interest is the report of du Vigneaud et al.¹⁷ To a diet highly protective against butter-yellow tumors, sufficient egg white (avidin) was added to produce a borderline biotin (vitamin H, which is essential for many forms of plant and animal life) deficiency. One group of rats was fed the diet alone and another group received crystalline biotin in addition. No tumors were found in the biotin-deficient group, whereas hepatomas were found in the animals whose diet was supplemented by biotin. Addition or subtraction of certain of the essential dietary components is also instrumental in increasing or decreasing the incidence of other types of neoplastic disease in animals, such as leukemia and spontaneous breast tumors.^{18, 19}

Of interest in respect to other cancer in human beings is the relation of dietary deficiency (particularly of the vitamin B group) to such lesions as papillary atrophy and leukoplakia of the oral cavity.²⁰ There is further evidence that these changes are associated with disorders elsewhere, as is shown by a high incidence of achlorhydria and functional and organic changes in the gastrointestinal tract. Administration of yeast is occasionally followed by a complete or partial remission of the lesions and symptoms.

Physical and Chemical Agents

Physical agents. The importance of changes produced by physical agents as a factor in cancer

formation has been mentioned previously. It has been shown that injury produced by radiation, burns, sepsis or other irritants may predispose to the development of tumor. In this regard the effect of solar radiation or actinic rays in relation to skin carcinoma is of much interest. Statistics reveal that individuals who are exposed to the sun and other elements have a higher incidence of skin cancer than others.²¹ Persons living in southern climates fall within this category. Moreover, skin cancer is more prevalent in exposed parts of the body, such as the face and hands. To test this hypothesis the skin of mice has been exposed to ultraviolet light. Cancers were produced in that part of the skin exposed in a high percentage of cases.²²

Carcinogenic chemicals. To date approximately two hundred and fifty chemical compounds possessing carcinogenic potency have been synthesized.²³ They differ widely in the speed and in the consistency with which they produce cancer in the experimental animal. Dunlap and Warren²⁴ have shown that slight changes in structure are followed by major changes in activity. The relation of the carcinogens to industrial chemicals that produce cancer is well recognized and has been summarized in a previous report.²⁵ These substances are of importance because they provide a tool by which the process of carcinogenesis can be studied. Interest at present is greatest in those chemicals which possess properties similar to those which may possibly be formed in the body. Experiments on the metabolism of one of these carcinogens (1,2,5,6, dibenz-anthracene) have shown that it is excreted as a phenolic derivative in various species of animals.²⁶ This excretion product is non-carcinogenic and is apparently detoxified in the body. Discovery of the mechanism by which this takes place may prove of importance, especially since it may enable one to study the influence of various agents on the production and inhibition of tumors.

Tissue extracts. Attempts have been made to demonstrate a carcinogenic action in cell-free extracts of tissue and excreta from patients with cancer. Tumors have been produced in animals by extracts of liver as well as from the urine of both normal and cancer patients.^{27, 28} These findings must be interpreted with caution, but this mode of approach is an interesting one and may yield significant information in the future.

Tobacco tars. Because of the possible connection between tobacco and the production of cancer of the oral cavity and lung, many investigators have studied the carcinogenic effects of destructive distillates of tobacco and of pipe tar.^{29, 30} The results are variable depending on the method of preparation and testing, but it has been reported

that after painting rabbits' ears with the material, papillomas and in some cases carcinomas developed. Others,³¹ using different animals or different distillates, have reported negative results.

Hormones. Until recently, interest in hormones as etiologic factors in cancer has been focused on the breast and cervix. At the present time, however, new facts may shed further light on the problem. The estrogenic hormones have been shown to be responsible for the production of adenomas of the hypophysis,³² interstitial-cell tumors of the testes,³³ fibromyomas of the uterus³⁴ and carcinomas of the cervix³⁵ in certain strains and species of animals. On the other hand, removal of the ovaries in mice,³⁶ rats and guinea pigs³⁷ of susceptible strains leads to the formation of adrenal hyperplasias and tumors. The possible relation of estrogens to cancer of the breast and of androgens to cancer of the prostate in human beings are of great interest, but as yet there is no good evidence to prove the hypothesis.

OTHER STUDIES

Genetics

The effect of foster nursing on the augmentation or inhibition of spontaneous breast tumors in mice of high and low cancer strains has been referred to in a previous report.²⁵ Prior to this finding it was not possible to produce cancer of the breast in males of low tumor strains by the administration of estrogenic hormone. However, the nursing of these males by mothers with a high cancer incidence, combined with the injection of estrogenic hormone, has resulted in the appearance of a significant number of cancers of the breast.³⁸ Spontaneous pulmonary tumors are unaffected by foster nursing, but there is evidence that the incidence of leukemia in susceptible strains can be altered by this procedure.³⁹ The factor responsible has been found in both the milk and blood of the animals.^{40, 41} Its exact nature is unknown.

Heterologous Transplantation of Human Tumors

Greene⁴² demonstrated several years ago that rabbit cancer could be transferred readily to animals of alien species by utilizing the anterior chamber of the eye as an inoculation site. Since that time he has successfully transferred a considerable number of human sarcomas and carcinomas to guinea pigs and rabbits. The value of such work is obvious, since it not only permits a study of the character of tumor growth, but may also provide information concerning the mechanism of carcinogenesis.

Viruses

This field of cancer is almost entirely confined to animal experimentation. Of interest is the iso-

lation of a specific material from virus induced cottontail-rabbit papillomas. It behaves histologically as the virus responsible for the disease, and has proved to be a nucleoprotein obtainable in solutions of high homogeneity.⁴³ This evidence suggests more than ever the chemical nature of the carcinogenic property of certain viruses. In connection with nucleoproteins it has been suggested⁴⁴ that these compounds are extremely important in determining growth because of their great chemical stability in nongrowing tissue and their high reactivity in growing tissue.

Immunity

So called "immunity" to tumors has claimed the attention of many investigators. Certain tumors in animals regress spontaneously or after transplantation and growth, whereas in other cases, immunity to subsequent growth can be induced by preliminary inoculation of a tumor or by non-specific measures, such as castration and injection of certain hormones.⁴⁵⁻⁴⁸ The Brown-Pearce carcinoma of testicular origin in the rabbit is easily transplantable and thus lends itself readily as a test object. Intracutaneous transplantation of the tumor results in a lesion that grows to a certain size, regresses, and renders the animal immune to subsequent transplants of the same neoplasm except in the anterior chamber of the eye.⁴⁷ In addition, intracutaneous transplantation of the tumor in an animal that already bears the same carcinoma and in which it is metastatic throughout the organs causes regression of all the lesions except those in the anterior chamber. Evidence accumulates that the inhibition is due to complement fixing antibodies developed in the animal and present in the blood serum.⁴⁸⁻⁵⁰ The ability of lesions in the anterior chamber to withstand such an antibody is apparently due to the barrier that exists between the blood and the aqueous humor. Similar possibilities in human tumors must be considered.

CLINICAL FACTORS

One hears the statement that little more can be expected of our present day methods of treatment of cancer. This is true if one does not take advantage of the knowledge gained in the recognition and behavior of the disease. Advances in other branches of medicine have, in an indirect fashion, contributed significantly to the problem. Cognizance of the facts and intelligent use of such information should enable one to utilize the methods at one's disposal with a greater prospect of cure. This is evident from the great strides that have been made in the treatment of cancers of certain organs that were formerly considered incurable.

Advances in anesthesia and an increasing knowledge of the physiology of the contents of the chest now enable the surgeon to enter the thoracic cavity with as much confidence and ease as when he enters the abdominal cavity.

Carcinoma of the pharynx and esophagus Wookey⁵¹ has reported on the successful removal of the hypopharynx and upper esophagus for carcinoma in 4 subjects, with excellent functional and cosmetic results. This operation was devised primarily to eradicate lesions that were not amenable to radiation therapy. Two of the patients were free of the disease at the time of the report, and the others had died of persistent or metastatic disease.

Carcinoma of the esophagus has taken a heavy toll, and until recently it has been considered a hopeless disease. Few cures have been reported by either radiation or surgery. Esophageal cancers are usually of the squamous-cell type, which should respond well to radiation. However, the organ is hollow and thin walled so that perforation into the mediastinum even after regression of the lesion is of common occurrence. Surgical extirpation has been frequently attempted, but until recently it was successful in only a few cases. Churchill⁵² has summarized the surgical aspect of the problem in a recent report. Advances in diagnostic, physiological and technical knowledge have made possible the successful removal of suitable lesions in a fair number of cases. Garlock⁵³ states from his own experience as well as that of others that the average patient with a carcinoma of the middle third of the esophagus stands a 54 per-cent chance of surviving the operation and a 30 per cent chance of living more than one year. With lesions of the lower third there is approximately a 70 per-cent chance of surviving the operation and 100 per cent probability of living more than two years. These figures refer only to operable cases, and failures in the group are frequently due to lymph node involvement.

Carcinoma of the lung. This condition is definitely increasing and at present ranks among the highest of causes of death from cancer. The reason for this is not clear, but it is believed that tobacco-smoking, tarred roads, fumes from combustible fluids or the influenza epidemic of 1918 may be contributory. It has been stated by several observers that the problem of cancer of the lung is not very different from that of cancer of the stomach. In fact, the resectability rates and the cures after successful surgical procedures are almost the same. The main difference is the higher mortality rate in surgery of the lung.⁵⁴⁻⁵⁵ The five year survivals in both groups are still considerably below those of most types of cancer. Metastasis to the regional lymph nodes and to re-

mote sites in addition to local extension renders many cases incurable. This is due in part to the fact that the disease is seldom diagnosed in its early stages. It is reasonable to assume that, when the local process is technically operable, metastasis or extension has not taken place. It has been pointed out that all patients having primary cancer of the lung without evidence of local extension or distant metastasis should have an exploratory thoracotomy to determine operability. This may be aided preoperatively by artificial pneumothorax. These measures are especially valuable since x-ray examination alone frequently gives an erroneous impression of the size and extent of the tumor.⁵⁶

Because radiation therapy has been disappointing, more frequent attempts at surgical removal have been made and are increasingly successful. The ideal operation, which consists of total removal of the primary growth and block dissection of the regional lymph nodes as in carcinoma of the stomach, breast and so forth, is not technically feasible. It is the consensus that total pneumonectomy, which may permit removal of the primary lymph nodes, is the procedure of choice in spite of the high operative mortality. Lobectomy may be used for a limited group with peripheral tumors and without gross involvement of the regional lymphatics. This is surgically and anatomically a poorer procedure than total removal of the lung.

Carcinoma of the stomach. Like cancer of the lung, there is an extremely high incidence of this disease. The introduction of improved and new methods, particularly that of gastroscopy, has considerably improved diagnoses, thus increasing the number of cases suitable for radical curative procedures. Of particular importance is the problem of the gastric ulcer. In general there has been a lack of understanding of the possibility that many of these lesions are malignant. As Gray⁵⁴ has pointed out, "It is not really so important to quibble as to whether or not a particular lesion was once a benign ulcer as to attempt to determine immediately whether or not the lesion under consideration is malignant." Mallory⁵⁷ has demonstrated that peptic ulceration of carcinomatous tissue in the stomach is not uncommon. It is assumed that it occurs in the early stages when secretion is fairly normal. This suggests that certain ulcers of the stomach are cancer to begin with and may in the early stages fall into the category of lesions known as cancer in situ.

Because of the difficulty in the differential diagnosis between gastric ulcer and cancer, the recent contribution of Allen and Welch⁵⁸ is of significance. From a statistical analysis of 277 cases in which the original diagnosis was gastric ulcer, 39 cases (14 per cent) finally proved to have cancer,

whereas 17 patients (6 per cent) with a preoperative diagnosis of cancer proved to have a benign ulcer. The approximate incidence of cancer in ulcers at various sites in the stomach has been stated by them to be as follows: greater curvature 100 per cent, prepyloric area 65 per cent, anterior and posterior wall 20 per cent, pyloric valve 10 per cent and lesser curvature 10 per cent. On the basis of these studies, Allen and Welch have made the following recommendations, which will bear repetition. Immediate surgery is recommended for any one of the following reasons: the ulcer is of short duration and the patient is over fifty years of age; the ulcer is over 2.5 cm. in diameter; there is no free hydrochloric acid in the stomach; the ulcer is in the greater curvature or in the prepyloric region; it is chronic and on the lesser curvature. Hospital observation and treatment for one month is recommended if the ulcer is acute and in a young patient, is under 1 cm. in diameter, or is on the lesser curvature or the anterior or posterior wall. If healing is complete in one month, the patient should be studied one month after discharge from the hospital. If healing is not complete in one month by roentgenologic or gastroscopic examination, then surgery is advisable. Allen and Welch conclude therefore that gastric ulcer is fundamentally a surgical lesion, that it cannot be distinguished from cancer in a high percentage of cases, and that gastric cancers which simulate gastric ulcers are an especially favorable group for cure. The end results of gastric resection from ulcer seem to substantiate this same form of treatment even if the ulcer is proved to be benign. These opinions are agreed with by most surgeons who have had an extensive experience with such lesions.

Increased knowledge of the mode of spread of carcinoma of the stomach, coupled with physiological advance and improvement in surgical technique, has widened the scope of treatment of the disease, especially as regards cases suitable for operative removal. Subtotal gastrectomy definitely limits the number of cases that can be cured. Removal of the omentum increases the possibility for cure, since it includes additional lymph nodes which may be invaded by the disease. Of late there have been an increasing number of successful total gastrectomies for lesions which were previously considered inoperable because of their extent and location. This applies particularly to lesions of the cardiac end of the stomach.⁵⁹ With the increasing incidence of successful resections for carcinoma of the lower third of the esophagus, interest has been renewed in lesions of the cardia.

Garlock⁶⁰ stresses that the biopsy report is of great value in determining the approach to lesions in the region of the cardia and lower third of the

esophagus. If the lesion is of the squamous-cell type it is probably of esophageal origin, whereas adenocarcinoma suggests an origin in the cardia of the stomach. These tumors are definitely different in respect to their mode of spread, and therefore a different surgical approach is indicated. Garlock states that on the basis of combined experience of various authors the patient with a resectable cancer of the upper end of the stomach has a 60 per-cent chance of surviving the operation and an 80 per-cent probability of living more than two years.

MISCELLANEOUS TOPICS

Hormones

The accumulation of information concerning the action of various hormones on specific organs, especially as regards their stimulating and inhibiting properties, has called attention to their possible significance as etiologic or therapeutic factors in neoplastic disease. Furthermore, studies of excretion rates of the sex hormones in the urine have provided valuable leads with specific types of tumors.

The most striking relation of hormones to a carcinoma of an organ normally acted on by the sex hormones has been provided by Huggins⁶¹ and his colleagues in carcinoma of the prostate. This has been the subject of a recent report by Quimby.⁶² It is well known that osseous metastases from cancer of the breast frequently regress in a most dramatic fashion following castration by either surgery or radiation. This has resulted in diminution of pain and in younger persons has slightly increased the life expectancy, but has had no effect on the subsequent course of the disease. By contrast, the results following orchidectomy for cancer of the prostate are much more encouraging, although it is too early to forecast what can be eventually expected from the procedure.

Recently Farrow and Adair⁶³ reported on the effect of orchidectomy in a man of seventy-two with cancer of the breast. There was complete relief from bone pain and evidence of increased calcification and healing of the metastatic bony deposits. The primary lesion, which had no treatment, also seemed to decrease in size.

Injection of hormones in an attempt to inhibit the progress of breast cancer has also been attempted.⁶⁴ The administration of either estrogens or androgens as measured by clinical, laboratory and radiologic findings caused an increased bone absorption, an elevation of serum and urinary calcium and increased activity in bone metastases. This did not occur in persons without skeletal dis-

ease. This is of extreme interest when compared with cancer of the prostate and its metastases, since estrogens in these lesions appear in some cases to augment the effect of orchidectomy, whereas androgens have proved deleterious.

Excretion of Sex Hormones

Carcinoma in general The findings of several investigators who have studied the urinary excretions of the sex hormones in patients with carcinoma of all types may be summarized as follows:

Gonadotropic hormones (pituitary origin)—There is no consistent pattern of excretion. Variations from normal may be correlated more closely with the physiologic state of the individual than with the presence of a carcinoma.

Estrogens (female sex hormones)—Pincus and Pearlman⁶⁵ report from their studies on pooled specimens of urine that the estrogen excretion in women with cancer is lower than that of normal women. In men this incidence was reversed and was thought to be due to a specific increase in one type of estrogen (estrinol).

Androgens (male sex hormones).—With few exceptions most studies of the androgens have been confined to the excretion rates of the 17 ketosteroids, which probably represent not only the biologically active androgens, but also closely related catabolic products of these and similar compounds that are not active in their excreted form. Pearlman,⁶⁶ Dobriner⁶⁷ and Nathanson⁶⁸ all agree that as compared with normal persons, patients with cancer have a lowered excretion of these compounds. Recent studies by Dobriner⁶⁷ and Pincus⁶⁹ further indicate that these compounds are not excreted in a normal relation with one another. There is evidence that several of the substances that are excreted by normal persons are absent from the urine of cancer patients. Several other compounds not previously identified have been found in the urine of those with neoplastic disease.

Specific lesions Carcinoma of the breast—Ross and Dorfman⁷⁰ could find no variation from normal in the estrogen and androgen excretion of women with cancer of the breast. Taylor⁷¹ and Nathanson⁷² found lowered estrogen and 17 ketosteroid secretion rates in similar patients as compared with normal women of the same age group. The differences were not considered as significantly altered from normal, since abnormal physiologic states due to other factors may have been responsible. Yolton and Rea⁷³ studied these excretions in 2 men with cancer of the breast, but found no difference from others of the same age. It can be concluded from these studies that the excretion levels of the sex hormones give no true index of

these agents in cancer of the breast. They do indicate, however, that the cancer may be initiated and maintained in the presence of normal hormonal levels.

Carcinoma of the prostate.—Scott and Vermeulen⁷⁴ found that before castration the level of 17-ketosteroid excretion in patients with cancer of the prostate was well below that of normal males of a younger age, but very close to levels for normal men of the same age and castrates. Castration leads first to a fall in 17-ketosteroids, followed by a rise. Estrogen excretion is low and decreases still further after castration. Castration leads to a moderate rise in urinary gonadotropins, which is slight compared to the values reported for younger castrates.

Testicular tumors.—It was formerly thought that the levels of the urinary excretion of anterior-pituitary-like hormone found in patients with testicular tumors paralleled the rapidity of growth and the grade of malignancy. Evidence by Twombly⁷⁵ indicates that there is no direct correlation between the excretion rate and the type of tumor. There is a suggestion of correlation with the prognosis of the disease. Cases that excrete 10,000 mouse units or over more than once are invariably fatal.

Functioning tumors.—Excretion levels of the sex hormones may be of distinct value in the diagnosis of functioning tumors of endocrine origin.⁷⁶ For example, differentiation of three types of tumors in females that produce similar syndromes may be aided by these studies. Patients with pituitary basophilism may excrete increased or decreased amounts of gonadotropins; the estrogens may be normal or lowered and the 17-ketosteroids within normal limits.^{68, 77-79} In adrenal hyperplasia the gonadotropic hormones are usually normal, the estrogens normal or elevated, and the 17-ketosteroids moderately elevated.^{68, 77, 78} As regards the 17-ketosteroids there is usually a normal relation between the various components.⁷⁷ It is believed that the 17-ketosteroids arise from both the adrenal glands and the gonads. There are two main groups: the alpha, which are probably of both adrenal and gonadal origin, and the beta, of adrenal origin only. They are usually excreted in a definite relation, that is, alpha 85-95 per cent, beta 5-15 per cent. In adrenocortical carcinoma the estrogens may be significantly elevated, but the most striking finding is a marked increase in the 17-ketosteroid excretion.^{68, 77, 78, 80} Moreover, there is a distinct shift in the relation between the components,^{67, 77} that is, a marked increase in the beta fraction, which may exceed 50 per cent of the total excretion. This is of the utmost importance in the differentiation of benign hyperplasia from cancer of the adrenal cortex. Men with pituitary basophilism

and boys with adrenal tumors exhibit the same excretion rates as the females. In men with adrenal tumors, feminization usually occurs, and this is reflected in a marked increase in the excretion of estrogens and normal or slightly elevated 17-ketosteroids. Arrhenoblastoma of the ovary gives variable results. Generally the estrogens are lowered and the 17-ketosteroids are normal or slightly elevated.^{68, 78} Granulosa-cell tumors of the ovary usually result in the excretion of large quantities of estrogenic hormone, but this is not necessarily true in all cases.⁶⁹ As more cases are studied these preliminary findings are certain to be clarified, and may prove of significance in the study of neoplastic disease.

METHODS OF THERAPY

Chemosurgery

Mohs⁸¹ has developed a new technic for the treatment of certain neoplasms, which he terms "chemosurgery." The idea originated from the well-known use of and occasional cure from caustics and fixatives employed by cancer quacks. This method involves chemical fixation of tissue with any of a number of agents. Briefly the method is as follows: The fixative is applied to the surface of the tumor, the dose depending on the penetration desired. Twenty-four hours later the fixed tissue is excised surgically; this can be done with a minimum of bleeding. The removed tissue is sectioned, and the location of cancerous areas is determined. Thereafter there is a daily repetition of the process, but only the neoplastic areas are treated until a microscopically noncancerous plane is reached. Mohs states that the main advantage of the technic is that it enables extirpation of an accessible neoplasm with unprecedented reliability, since it includes all unsuspected extensions and produces a minimal destruction of tissue. The method requires special training and painstaking control. Mohs reports a large series of patients with cancer of the skin, lip and so forth who have been free of disease for one to four years, but makes no claims as to its greater efficacy as compared with other methods in effecting a permanent cure.

Refrigeration

It is now generally agreed that refrigeration is of no particular value in the treatment of cancer, except in so far as it may produce a diminution of pain. The difficulties of the method, the complications and dangers of its use such as pneumonia and cardiac failure and the efficiency of other measures for the treatment of the lesion and relief of pain relegate this type of treatment to a few selected cases where it may be worth a trial.

Radiation Therapy

The use of x-rays, radium and radioactive isotopes in the therapy of cancer has been reviewed by others.^{82, 83} in this series. It may be added that Donovan and Warren⁸⁴ have shown that the intracavitary use of radium in cancer of the endometrium is seldom effective in completely eradicating the disease. In the past few years, the use of intracavitary x-rays by means of special cones has been a most valuable adjunct in the treatment of cancers of the oral cavity, bladder and cervix, when combined with the usual methods of external radiation.

Treatment of Pain

Advances in neurosurgery have helped considerably in combating the pain from cancer. There have been many reports regarding effective procedures. Grant⁸⁵ has summarized and presented data on what can be done for the relief of pain by interruption of the sensory pathways, discussing the hazards involved and the justification for the procedures. Decisions must rest on the site and rate of growth of the tumor, the life expectancy, the degree and location of pain, the general condition of the patient as an operative risk and the amount of sedation or opiate necessary for relief. Grant discusses the indications for and results of such procedures as subarachnoid injection, nerve section, chordotomy and rhizotomy. Results from these measures are most encouraging. Munro⁸⁶ is of the opinion that the development of pain in cancer of the head and neck is associated with the effect of x-ray therapy. He advocates surgical denervation of the cancer-bearing areas in selected cases as the first step in the treatment of the disease, to provide against possible subsequent pain and as an aid to more efficient therapy. Reports on the use of cobra venom are variable, but it seems to be worth a trial in selected cases. All authors rightly deplore the indiscriminate use of morphine in cases of terminal cancer, especially because of the fact that the symptoms due to addiction far outweigh the pain produced by the disease.

METASTASES

An increase in the number of cases in which the primary cancer has been controlled has resulted in concentrated studies on the modes and sites of metastases from various organs. This is necessary since therapy must now be directed more rigorously toward these secondary deposits in an effort to effect a complete cure of the disease. Willis⁸⁷ has supplemented his original classical monograph on the spread of tumors and points out the more likely routes and location of the disseminated tumor. Other investigators have been primarily

concerned with lymph-node metastases which are amenable to treatment. Of particular interest is the utilization of the Spalteholz clearing method by Gilechrist and David⁸⁸ and Coller et al.^{89, 90} to study the incidence and sites of metastatic nodes from various lesions of the stomach, colon and rectum. It has been demonstrated that the number and extent of nodes involved are far greater than was formerly realized. Duffy⁹¹ and Martin⁹² have confined their work to lesions of the oral cavity. A comprehensive study of the problem based on an analysis of almost 6000 cases has been made by Taylor and Nathanson.⁹³ On the basis of their findings, combined with the experience of others, they have set down criteria for diagnosis and methods of management of the common and many of the rarer types of tumors.

CANCER CONTROL AND PUBLIC-HEALTH PROGRAMS

The Massachusetts Department of Public Health continues its program of education. Teaching clinics are held frequently at various centers throughout the state. This program has been of inestimable value, since it has resulted in earlier and better diagnosis, improved treatment and a decrease in the delay before treatment is instituted. Even though the cancer rate has increased, the morbidity and mortality from the disease have shown a relative decline. The American Society for the Control of Cancer is now aided by the Women's Field Army in its campaign. The latter organization has been effective in raising money to provide more efficient facilities for the care of the patient and for education. Many other states, as well as the federal government, have adopted progressive programs. In addition, new institutes and hospitals have been opened. Notable among these are the National Cancer Institute at Bethesda, Maryland, where research in cancer is carried out, the new state hospital in Missouri and a proposed hospital in Texas.

In order to care for persons in the western part of Massachusetts and to relieve the burden on the Pondville Hospital, the Commonwealth has built a 50-bed addition for cancer patients at the state tuberculosis sanatorium at Westfield. One of the pioneer institutions, the Collis P. Huntington Memorial Hospital, has closed its doors because it was thought that it could serve the community more effectively if it were a part of a large general institution. Its functions, including its clinical and research facilities, have been transferred to the Massachusetts General Hospital.

Periodic Examination

There has been much interest in periodic examinations of persons who are in the cancer age. The

efficacy of this program is apparent from the report of MacFarlane,⁹⁴ who has made semiannual pelvic examinations in 1000 women over the age of thirty. In the past three years, 4 early unsuspected cases of cancer of the cervix and fundus of the uterus and 119 lesions of the cervix that were believed to predispose to the development of cancer were found and treated.

* * *

This review of some of the more pertinent material on cancer for the past few years has aimed to give the physician a broad view of the problem as a whole. The details of each type of approach may be learned by consulting the references. It should be realized that much is known of the etiology, diagnosis and treatment of cancer, and it is hoped that the pessimistic attitude so often held will be reversed. The future is promising, but even at present we have at our disposal potent weapons which, if used intelligently and judiciously, will do much to combat effectively a major disease of our aging population.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28481

PRESENTATION OF CASE

First admission. A seventeen-year-old Italian-American girl was admitted to the hospital because of headaches for four weeks.

She was in good health until one evening five weeks before entry, when she went for an hour's ride in an automobile. In the course of the ride the right side of her face was exposed constantly to a cold wind. She also struck the right side of her head against the top of the car, but only hard enough to cause momentary discomfort. Later in the evening there was some twitching of the right side of the face. The next morning, her mouth was "crooked," and she was unable to blink her right eye. She was seen in the Emergency Ward, where she seemed quite weak, and twice tended to faint; she did not, however, lose consciousness.

Examination showed partial paralysis of the entire right side of the face. There were no sensory changes, but slight tenderness was noted in the region of the right facial canal. She was given 75 mg. of thiamine chloride by intravenous injection, and rest was recommended. Eight days later, she returned to the Out Patient Department, complaining of an ache in the right ear induced by loud noises. The facial paralysis was unchanged, and there was, in addition, slight hypalgesia over the right side of the face. A roentgenogram of the skull showed normal convolutional markings and normal configuration of the sella. The left acoustic meatus appeared slightly larger than the right. Five days later, the patient was given massage and electrical physiotherapy for her persistent facial palsy. At about this time she began to complain of "occasional" right frontoparietal headaches, which were sometimes "knifelike" and sometimes "pulling." Twenty-four days after the patient was first seen, facial muscular function was found essentially normal and an audiogram showed bilateral normal hearing. In the next two weeks, the patient experienced headaches of increasing severity. She felt "peppless," easily fatigued and

without appetite. The night before entry, she had some "difficulty in breathing."

The family history was not of interest. The patient had been seen in the Out Patient Department when thirteen years old for a suspicion of rheumatic fever, but this diagnosis had been rejected. At fifteen years she had again consulted the clinic because of increase in size of her right breast, with slight pain, unrelated to the menses; some hypertrophy of breast ducts had been observed.

Examination disclosed an apparently healthy girl. The right breast was slightly larger than the left. A few lymph nodes were palpable in the neck. The heart, lungs and abdomen were not remarkable.

The blood pressure was 130 systolic, 80 diastolic. The temperature was 100°F., the pulse 100, and the respirations 20.

On neurologic examination, the pupils were equal, but reacted with hippus. The fundi were normal. The visual fields and blind spots had normal configuration. Tests of smell, hearing and taste were negative. There was slight hyperesthesia over the right temporoparietal area, but no other sensory disturbance. The reflexes were physiologic. A slight residual peripheral right seventh-nerve paresis remained. A lumbar puncture gave clear colorless fluid under an initial pressure of 140 mm. of water. The total protein was 25 mg. per 100 cc.; the gold-sol curve was 0011100000, and the Wassermann reaction was negative. An electroencephalogram was negative.

The examination of the blood, including a Hinton test, was negative. The urine also was not remarkable.

During the stay in the hospital the patient's temperature varied irregularly from 98 to 100°F. On the eighth day a slight swelling was noted in the right temporoparietal region. On the tenth day the patient complained of numbness over the right side of her face. The next day she was discharged.

Second admission (nine and a half weeks later). Following discharge the patient was followed for the next five weeks in the Out Patient Department. Her headaches continued as before. Because of a slight increase in the temporoparietal swelling and persistent tenderness in this area, another roentgenogram of the skull was taken. This showed a sharply outlined defect in the right frontal bone, just anterior to the coronal suture, measuring 3 by 2 cm. (Fig. 1). Except for this palpable, slightly tender defect, physical examination was as noted on the first admission.

The temperature was 98.6°F., the pulse 80, and the respirations 20.

The blood and urine were again essentially negative. The blood cholesterol was 134 mg., the calcium 11.7 mg., the phosphorus 2.9 mg., and the phosphatase 1.7 Bodansky units per 100 cc. Roentgenograms of the chest and of the renal tract (pyelograms) were negative. Another roentgenogram of the skull, taken six and a half weeks after the previous one, showed slight increase in size of the bony defect. The outer table of the skull

there was only a mild residuum at the time of admission.

Slight swelling in the right temporoparietal region developed, which was noted to be tender at the time of the second admission (nine and a half weeks after the first admission).

Roentgenograms of the skull seven weeks after the onset of symptoms showed a large, punched-out defect involving the right frontal bone—this despite the fact that roentgenograms of the skull nine weeks before had shown no evidence

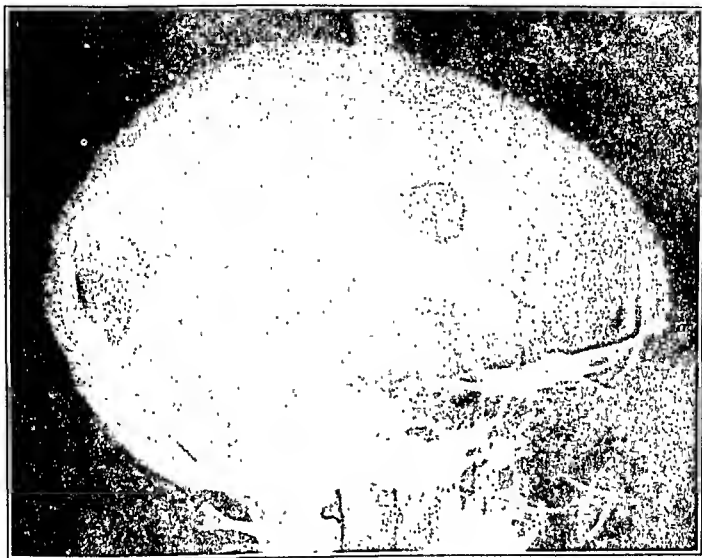


FIGURE 1.

was involved to a much greater extent than the inner. On the fifth hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM T. GREEN*: The five most pertinent factors in the history may be listed as follows:

A seventeen-year-old girl was admitted with a primary complaint of right frontoparietal headache of three weeks' duration.

A facial paralysis on the right occurred suddenly one or two weeks before the onset of the primary complaint and improved so rapidly that

of this lesion and, in fact, were interpreted as normal except for a questionable narrowing of the right internal auditory meatus.

The patient was apparently healthy except for the specific complaints that have been mentioned. The first examination confirms this impression. Neurologic findings were entirely within normal limits except for the facial weakness, indicating a lesion of the right seventh nerve. All recorded laboratory determinations gave normal findings.

We are primarily concerned in this diagnosis with the disease as represented by the destructive lesion in the skull. All other considerations are subservient to this one problem.

Let us consider the facial palsy. The question arises whether the facial paralysis is a part of the

*Assistant professor of orthopedic surgery, Harvard Medical School, visiting surgeon, Children's Hospital, Boston

general picture, or an incidental feature. Is the paralysis caused by the lesion that produced the area of destruction in the skull? Is the paralysis central or peripheral in origin?

The facial paralysis came on two weeks before the onset of the headache and five weeks before admission. It involved both the upper and lower portions of the face. It was right sided in distribution (the lesion in the skull was on the right side). This facial weakness came on suddenly with a history of an antecedent "bump" in the area, and on the night before it was noted the patient had ridden in an open car, her face on the involved side having been exposed constantly to a cold wind. I should assume that a tentative diagnosis of Bell's palsy of the ordinary type was made when she was first seen in the Out Patient Department. This paralysis improved rapidly so that a note was made three weeks after its onset that the weakness of the muscle had largely disappeared, although on admission to the hospital it is commented that some residual weakness remained.

In the course of this facial paralysis and before admission the patient complained of a hyperacuity in hearing with pain on noisy stimuli, which might suggest to an orthopedist—who knows nothing about it—that the nerve to the stapedius muscle was involved. One could state that the lesion was infranuclear, not supranuclear, in origin, since the upper facial distribution was involved just as much as the lower face. In supranuclear lesions, this is not true.

The second question, granting that the lesion is infranuclear, is whether the lesion arose before the entrance of the facial nerve into the facial canal, or within the facial canal. If the lesion were in the cerebellopontine angle, one would expect to have involvement of other cranial nerves, including probably the eighth and sixth nerves. There was no evidence of this. In fact, the neurologic findings were entirely negative at all times except for the facial palsy. It is not stated that definite observations were made regarding taste when the facial palsy was marked, although later there was no disturbance in this sensation. All evidence, including the hyperacuity of hearing and the painful hearing on noisy stimuli, indicates that the lesion was peripheral or in the facial canal. Everything suggests that it was an ordinary Bell's palsy, particularly since the lesion improved at quite a rapid rate, but there is one other possibility to be considered as an etiologic factor, which we will discuss later.

Roentgenograms of the petrous portion of the bone were reported as essentially negative, although there is some question whether the internal auditory meatus on the right side was not smaller

than that on the left. I judge that there was no strong feeling about it. I hope that Dr. Holmes will comment on these findings later.

The headache, I believe, was related directly to the lesion that was later demonstrated to be present in the skull, since the site of the discomfort coincided with the position of the lesion. However, on the first admission, the headache could not be explained and the lesion had not been demonstrated. The only significant finding was that, on the patient's eighth day in the hospital, there was a suggestion that she had some swelling in the right temporoparietal region, but it apparently did not cause particular concern and she was discharged.

On the second admission, nine and a half weeks later, the physical findings were essentially the same except that there was more swelling in the temporal area and roentgenograms showed a definite defect. Perhaps we could have the roentgenograms presented at this time.

DR. GEORGE W. HOLMES: I should be inclined to agree with Dr. Green, that the first x-ray interpretation was an attempt to find something,—an attempt to call attention to a possible variation,—but the examiner was not very certain about it. The second time there was a very definite lesion that was not present the first time. It is a sharply defined area of destruction of bone, which occupies a considerable area.

DR. GREEN: I wondered about the relative density and aeration of the mastoid process on each side. How do you account for the difference on the two sides? On one side, there is moderate aeration, and on the other there is increased density.

DR. HOLMES: The patient could have had infection on the denser side.

DR. GREEN: An old sclerosing process?

DR. HOLMES: Yes.

DR. GREEN: But there is no evidence that such infection existed. I imagine that the interest in this patient increased a great deal when the roentgenograms revealed the area of destruction in the skull on readmission. Probably the question was whether the facial palsy arose from the lesion in the skull, but I have pointed out previously that the facial palsy was not supranuclear in origin and, as a matter of fact, if the lesion was a factor in the facial palsy the paralysis would have been on the opposite side, namely, the left.

At the second admission, the patient had a destructive lesion of the skull associated with headache, but there was little general illness. The term "pain" was never used in a description of her complaints. Roentgenograms of the chest were interpreted as normal; there was no evidence of met-

astatic lesions. I assume that there were no other bone lesions, although there is no note that roentgenograms of the remainder of the skeleton were made. Were they taken?

DR. TRACY B. MALLORY: They were taken and were negative.

DR. GREEN: In analyzing the lesion in the skull, certain comments should be made. One always thinks of infection when there is destruction of bone. From the roentgenographic appearance, it is possible that this lesion might have arisen from infection. It is not likely, however. Clinically there was no evidence of it. There were no particular febrile episodes. Tenderness was minimal, and there was no reaction over the lesion. In roentgen appearance it is too clean-cut and smooth and does not show enough reaction in the surrounding bone to be compatible with ordinary pyogenic infection. So far as other types of infection are concerned, one might mention syphilis, but we are not concerned with it as a possibility. In fact, I do not believe that the lesion was due to infection.

Was it a tumor? Various possibilities must be considered, but I think that we can cut short our discussion of these in deference to time. I should say that the destructive area gave little evidence of actual tumor. It must have been quite flat since, when it was talked about after it was noted, it was commented on as a defect. Most tumors of ordinary type grow in a centrifugal concentric fashion, and according to the outline as seen in the skull, if the lesion were a tumor growing in such fashion, there would have been a considerable mass.

I shall not comment on the various types of tumors that this lesion might represent, except to say that I do not believe it is tumor, either primary or secondary.

I might make some comment about the possibility of multiple myeloma. Ordinarily a lesion of multiple myeloma is likely to be smaller than this, but even larger lesions occasionally occur. The patient's age, however, is important. She was seventeen years old, and although multiple myeloma is described in even younger persons, these alleged cases with which I am familiar are open to question.

We then arrive by elimination at the particular disease that I believe this patient had, namely, Hand-Schüller-Christian disease¹—xanthomatosis is a synonymous term. The typical Hand-Schüller-Christian syndrome has come to be associated with multiple destructive lesions of the skull, particularly those which are geographic in type and sharply punched out, exophthalmos and diabetes

insipidus. We know, however, that the latter two features of the syndrome are really due to the location of the lesions in the skull. The diabetes insipidus depends on a lesion involving the region of the sella turcica and the base of the third ventricle; and the exophthalmos is dependent on a lesion that involves the orbital plate. The fact that this patient had neither diabetes insipidus nor exophthalmos does not affect my decision regarding this particular patient.

A couple of years ago, two articles came out within a short time of each other—one "Eosinophilic Granuloma of Bone," by Lichtenstein and Jaffe,² and the second "Solitary Granuloma of Bone," by Otani and Ehrlich.³ Both these articles describe the same type of granulomatous process. I will not comment on the process further except to say that it is characterized by the presence of a large number of eosinophils and large monocytes that show inclusions. During the last twelve years, I have followed quite a few patients with lesions of the type that they described. Dr. Sidney Farber and I⁴ have reported 10 of these, and in all we have seen 16. I shall leave it to Dr. Mallory to discuss the pathologic picture in this type of disease.

DR. MALLORY: Go right ahead.

DR. GREEN: The lesions that we have seen were single in certain patients and multiple in others. In the 10 patients reported, there were single lesions in 4 and multiple lesions in 6. The lesions of the bone were more frequently seen in the skull and in the ribs. The vertebral column and pelvis were involved quite frequently, as well as the long bones. The patients showed a relatively benign clinical course. However, we have seen other patients with similar bone lesions histologically and roentgenographically who also had visceral manifestations; the prognosis in such a case is not good. In the latter group, all patients had visceral manifestations as well as bone lesions at the time we first saw them. The condition in this group may be classified as Letterer-Siwe disease.⁵ Dr. Farber believes that Hand-Schüller-Christian disease and eosinophilic granuloma represent the same fundamental type of pathologic process and, in fact, that Letterer-Siwe disease—that is, the type with visceral involvement—is likewise related.

The patients with eosinophilic granulomas have shown a good response to x-radiation, but I suggest that it should be given in relatively small doses to the particular lesions and the effect should be carefully observed. One is tempted to give heavy doses, but in our experience this is not necessary and it is better to hold something in reserve, since

many new lesions may appear in the course of the disease. Certain of the lesions have healed spontaneously.

The cause of the disease is unknown; in fact the reason that our cases were not published sooner was that we were attempting to determine the etiologic factor responsible for the condition. It has been suggested that the disease might be due to a virus, but there is no proof at this time of such a causative agent.

In connection with the facial palsy, it is entirely possible that a very small lesion in the petrous portion of the temporal bone, which could not be seen in the roentgenograms, might have been responsible, since this bone is frequently involved by the process.

DR. MALLORY: Which of the multiple names do you choose to call it?

DR. GREEN: I do not know what we should call it, but we must call it something to know what we are talking about. We should know more about the etiology of the pathologic process in order to give it a suitable name. At the present time, we give the diagnosis: Hand-Schüller-Christian disease, eosinophilic-granuloma variant.

CLINICAL DIAGNOSIS

Lymphoma?

Metastatic malignancy?

Hand-Schüller-Christian disease?

DR. GREEN'S DIAGNOSIS

Hand-Schüller-Christian disease, eosinophilic-granuloma variant.

ANATOMICAL DIAGNOSIS

Granuloma of bone (Hand-Schüller-Christian type).

PATHOLOGICAL DISCUSSION

DR. MALLORY: The biopsy of this lesion showed a granulomatous process containing foam cells but no eosinophils. Histologically it was very typical of Hand-Schüller-Christian disease. I am entirely in agreement with Dr. Green and Dr. Farber in believing that all these conditions represent transitional forms of a single disease entity without known etiology. Usually the more typical xanthomatous processes are seen in the younger age groups, whereas the so-called "eosinophilic granulomas" are seen in young and middle-aged adults. However, I have seen a marked eosinophilic reaction without cholesterol deposits in a child of three, and marked xanthomatous reaction without eosinophils in a woman in her late forties. This patient was treated by x-ray, and the lesion partly filled in, although it never completely

disappeared. This film shows the situation two years later. She has been clinically free from symptoms.

DR. GREEN: The younger persons, of course, have an advantage in healing. The skull lesions in our patients showed complete healing. This girl was older, seventeen, and this might well account for the residual defect.

DR. FULLER ALBRIGHT: They removed the sum and substance.

DR. GREEN: That might well be a factor, but the substance was removed before the biopsy, if you can judge from the appearance of the film.

DR. MALLORY: Would you be enthusiastic about further treatment?

DR. GREEN: No; it is worth while stating that we have seen multiple lesions representing the various phases of the disease as we interpret them.

DR. JOSEPH C. AUB: Is it not unusual for it to develop so rapidly?

DR. GREEN: No; I have seen a skull treated in one area, and a month later a big new defect in an untreated area.

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CASE 28482

PRESENTATION OF CASE

A fifty-two-year-old businessman was transferred to the hospital for study of a disorder that began with a generalized feeling of weakness.

Approximately one and a half weeks prior to admission he contracted an upper respiratory infection, which seemed different from the usual variety. He felt exhausted, and remained at home several days longer than after an ordinary cold. Despite the added rest, he was quite tired when he resumed his normal activities. Several days later he complained of extreme fatigue. One evening he developed a tingling sensation in the tips of the fingers and toes and about the mouth. He was restless during the night and at 6:00 a.m. awakened and attempted to get out of bed but was very unsteady and fell backward against the bed. At this time his wife noticed that his speech was thick. There was ptosis of the right eyelid, and he complained of diplopia. His wife was obliged to help him to the bathroom because of the unsteadiness and the marked feeling of fatigue. His

physician examined him that morning and noted bilateral ptosis, some disturbance of eye movements and bilateral positive Babinski reflexes. That afternoon he entered a community hospital, when his physician noted more complete ptosis of the eyelids and reduced eye movements. There was bilateral weakness of the facial muscles, and the speech disturbance was more pronounced. The arms and legs were considered normal. However, the bilaterally positive Babinski reflexes persisted. He was seen in consultation six hours later, when he stated that he felt better, but complained of a sense of stiffness about the face. A nurse noticed that he had a progressively increasing difficulty in swallowing fluids during the afternoon and that he occasionally coughed because of inability to swallow the saliva. At no time were urinary bladder difficulties noted.

Physical examination revealed a slight cyanosis of the lips, but the lobes of the ears and the fingernail beds were normal in color. The respiratory movements of the chest and the diaphragmatic excursions seemed normal. Examination of the heart and lungs was negative. Neurologic examination showed bilateral, almost complete ptosis of the eyelids. Upward movement of the right eye could not be accomplished, but there was some movement laterally, medially and downward. The left eye moved through a slightly larger arc but was somewhat limited in all movements. The pupils were equal, with an aperture of approximately 1 mm., and reacted to light. The fundi were poorly visualized. The right optic disk was normal in size and outline, but hyperemic. Sensation of the cornea and skin of the face was normal. There was paralysis of the lower facial muscles, but the action of the frontalis was normal. The tongue was weakly extended in the midline to the edge of the lips. The palate lifted weakly in the midline. There was questionable weakness of the neck muscles, particularly the trapezius muscles, and the neck was not stiff. The abdominal reflexes were absent. The extremities were strong, and their movements well co-ordinated, as evidenced by the finger-to-nose and heel-to-shin tests. The tendon reflexes were hyperactive, and there were bilaterally positive Hoffmann and Babinski reflexes. No diagnosis was established, and the patient was immediately transferred to this hospital.

The family history was noncontributory. During World War I the patient suffered with influenza and was greatly debilitated by the illness, but there was no apparent permanent injury and no sequelae developed. During the subsequent years he contracted frequent upper respiratory infections, and many of these kept him from business.

During the months prior to the present trouble some general slowing-up of the patient's business activity was noticed but never to a degree considered important.

Physical examination confirmed the findings at the community hospital.

The blood pressure was normal. The temperature was 98.9°F., the pulse 69, and the respirations 26.

Examination of the blood revealed a hemoglobin of 13.6 gm. and a white-cell count of 18,000, with 87 per cent polymorphonuclears. When repeated four days later the white-cell count was 15,200. The blood nonprotein nitrogen was 28 mg. per 100 cc. The blood Hinton test was negative. The urine was negative. An x-ray film of the chest showed increased markings of the right upper lobe. There was no gross consolidation within the lung fields, and no displacement of the heart or mediastinum. A lumbar puncture showed an initial pressure of 160 mm. of water. The spinal fluid was clear and colorless and contained 400 red cells and 2 white cells per cubic millimeter. The total protein was 45 mg. per 100 cc.; the Wassermann was negative, as was the gold-sol curve. The chlorides were 723 mg. per 100 cc. Another spinal tap on the same day showed only 2 red cells per cubic millimeter.

That night he developed a distressing attack of hiccoughs, but at no time was there any respiratory difficulty. The following morning he felt and appeared improved. The left eyelid could be elevated more easily, and the ocular movements were better on both sides. The facial weakness had improved, and the tongue movements were better. Speech was less thick. The Babinski and Hoffmann reflexes gradually became negative during the second day. The tendon reflexes became somewhat sluggish, but strength remained good. Improvement continued during the next four days, and at the end of that time only the ptosis of the right eyelid and weakness of all the extraocular muscles remained. The strongest movement of the right eye was outward, and there seemed to be some dissociation in conjugate movements. The pupils were 3 to 4 mm. in diameter and reacted normally to light and accommodation.

On the evening of the fifth day, he again experienced some tingling of his fingertips and felt unusually tired. He slept well that night and ate a good breakfast the next morning. The attending nurse stated, however, that he was quite drowsy and less responsive than on the previous day. Approximately an hour after breakfast, when visited by his physician, he did not respond to a morning greeting. When approached more close-

ly, he mumbled, turned his head slightly to the left and "thickly" said that the numbness and weakness of his face had returned. At that time there were bilateral ptosis, a marked weakness of the lower facial muscles, inability to protrude the tongue and paralysis of the right hand and right leg. During the morning he became totally unable to speak but responded to pinprick by movement of the head and trunk. The left arm and leg could be moved on request. The pupils had again become very small. The neck muscles were weak. Tendon reflexes were more active on the right than on the left. The Babinski reflex was positive only on the left side. Respirations gradually became labored, and cyanosis developed. The patient began to drool. There was a marked tendency for periodic spells of hiccoughing and explosive coughing. On the seventh day, the temperature rose to 100°F., the bronchial tree filled with mucus, and the patient became very cyanotic and died.

DIFFERENTIAL DIAGNOSIS

DR. CHARLES S. KUBIK: The spinal fluid was negative except for a total protein of 45 mg., which is a moderate increase. I assume that the 400 red cells meant a bloody tap, since the fluid obtained at another puncture a little later contained only 2 red cells.

Ten days or so following the onset of what is said to have been an upper respiratory infection this fifty-two-year-old man rather suddenly began to have symptoms of cerebral disease. These progressed for a day or so and then improved somewhat; the patient seemed to be holding his own when he rapidly became worse, and died about one week after the onset of neurologic symptoms, or two and a half weeks after the time that his first illness began.

The description of the initial illness is too meager for one to attempt a diagnosis. It may or may not have been connected with what followed.

I should like to begin by discussing the cerebral symptoms, attempting first of all to make a localization, which, if it can be determined, sometimes gives a clue to the diagnosis. There were an abundance of focal signs, which were bilateral from the start, and most of these suggest disease of the brain stem. Ptosis, diplopia, ocular palsies point to the midbrain; bilateral facial weakness to the pons; dysphagia, inability to protrude the tongue, hiccough and weakness of the trapezii to the medulla. Involvement of the corticospinal tracts, indicated by extensor plantar responses, could occur at any one of these levels. It is not quite so simple, however, as I have made it sound. Why was only the lower part of the face para-

lyzed, and if there was nuclear facial and palatal paralysis, why was there no involvement of the fifth-nerve nucleus, with resulting sensory impairment on the face? One might have expected the vestibular nucleus to be implicated, with vertigo, nausea, nystagmus and unsteadiness of the extremities.

The rapidity with which symptoms developed at the time of the earlier episode and again shortly before death suggests arterial occlusion and infarction, and this diagnosis fits in with the blood supply of the parts under suspicion. The lateral portions of the medulla are usually supplied by branches of the posterior inferior cerebellar or vertebral arteries or both; its ventral and medial portions, by tiny branches of the anterior spinal and basilar arteries. The basilar artery supplies the greater part of the pons, and arising from its bifurcation are several small but important branches, which enter the midbrain anteriorly and supply, among other things, the third nerves, the region of third-nerve nuclei and at least part of the peduncles, through which the corticospinal tracts pass.

Since the optic thalami obtain their blood supply from the posterior cerebral or posterior communicating arteries or both, occlusion of the basilar artery might very well account for the paresthesia of fingers and toes and about the mouth. The posterior cerebral arteries also supply the visual cortex, and one might have expected impairment of vision or hemianopsia, although this would not occur if there was an adequate collateral circulation through the posterior communicating arteries. Small pupils are commonly observed with occlusion of the basilar artery.

Is remission consistent? We have observed it in other cases, and I believe that it may be explained by collateral circulation through the posterior communicating arteries. These are later blocked off by extension of the thrombus, when there is an exacerbation of the symptoms followed, in a short time, by death.

Rapidly increasing fatigue with subsequent cerebral symptoms might lead one to think of bacterial endocarditis, but there is nothing to support such a diagnosis. The onset of cerebral symptoms, moreover, which apparently was not altogether abrupt, was more suggestive of thrombosis than embolism.

DR. JAMES B. AYER: I am sorry that Dr. Kubik did not even consider the diagnosis that I made, and which to my surprise was wrong. This patient was of the right age to have contracted encephalitis lethargica, between 1918 and 1922, when this disease was epidemic. In one of the types of this disease it was not uncommon to see lesions

involving the brain stem, pathologically showing collections of small round cells and perivascular exudate, much of it in the gray matter, causing cranial nerve palsies; and it was characteristic of these palsies to vary in intensity and even to disappear during the course of the illness. The motor system was more affected than sensory. I should like to ask Dr. Kubik why he did not even consider this diagnosis.

Dr. KUBIK: I did consider it but did not say anything about it. In a case we had here a good many years ago with paralysis of ocular muscles as the chief symptom but with a longer history,

cranial-nerve palsy on the right, the next day on the left, and the next day on the right again.

Dr. KUBIK: As rapidly as in this case? There is usually a headache.

Dr. AYER: Not necessarily.

Dr. KUBIK: And drowsiness or confusion

Dr. AYER: Usually.

Dr. KUBIK: And cells in the spinal fluid

Dr. AYER: Very few.

Dr. KUBIK: Those were my reasons.

Dr. DAVID G. COGAN: By the time I saw the patient on the second day of his hospitalization the eye movements had already improved. How-

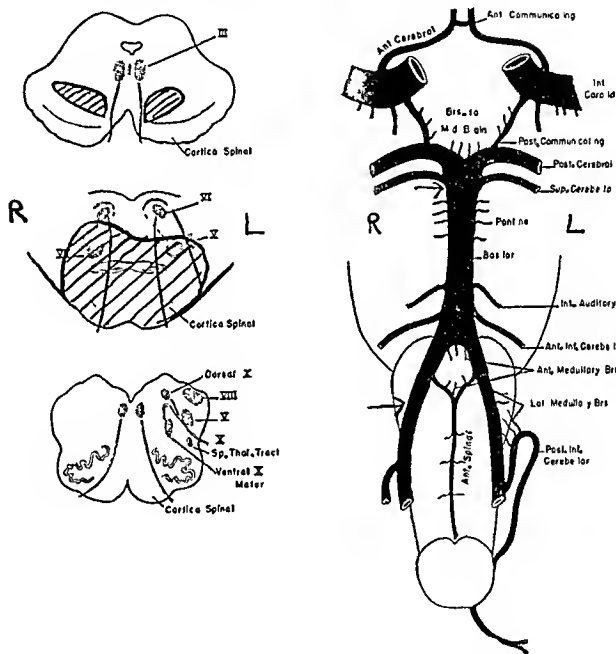


FIGURE 1

there was extensive degeneration of the myelin in the midbrain, corresponding to what has been called "acute multiple sclerosis," although I am not sure it is not a misnomer. In that case there was extensive perivascular infiltration, suggesting an infectious process of some kind, but not encephalitis lethargica. One of my reasons for excluding encephalitis was the fact that there were remissions and exacerbations.

Dr. AYER: It was quite characteristic to look at the encephalitic patient one day and to see a

ever, at that time he showed a paresis of conjugate gaze downward, upward and to the right. Conjugate movements to the left were normal. The only evidence of ocular palsy was weakness of the right inferior oblique muscle.

Dr. KUBIK: There was ptosis

Dr. COGAN: Yes.

Dr. KUBIK: On both sides.

Dr. COGAN: Chiefly on the right. The fact that he had a paralysis predominantly of the vertical conjugate mechanism makes one think the lesion

was in the anterior tectum. But the conjugate palsy to one side points to a pontine lesion. My impression, therefore, was that the lesion was a diffuse midbrain and pontine affair involving the ocular conjugate tracts and nuclei and not a peripheral-nerve lesion.

DR. MILTON J. QUINN: I was greatly impressed by the signs of general weakness. The patient did complain that the right leg was weaker than the other over a period of two weeks following the respiratory infection. When I saw him he had a shaking chill, and following that, his temperature rose to 100°F. Examination of the pupils at that time showed the right to be 4 mm., and the left 2 mm.

CLINICAL DIAGNOSIS

Encephalitis lethargica, bulbar type.

DR. KUBIK'S DIAGNOSIS

Thrombosis of basilar artery.

ANATOMICAL DIAGNOSES

Thrombosis of basilar artery.

Infarction of pons and midbrain.

Pulmonary congestion and edema.

Pericarditis, aseptic, fibrinous.

Arteriosclerosis, moderate: aorta and coronary and basilar arteries.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The primary lesion in this case was, as Dr. Kubik predicted, a thrombosis of the basilar artery. Since most of us cannot visualize the details of the cerebral blood supply with the vividness that he does, I suggest that we look at the diagrams (Fig. 1) as I describe the findings. The thrombus began in the right vertebral artery just above the origin of the posterior cerebellar artery and extended upward throughout the length of the basilar artery to approximately the point

of its bifurcation to form the posterior cerebral arteries, the two arrows indicating its respective ends.

From this point on I wish that Dr. Kubik rather than I had to describe the anatomic findings, since I cannot reconcile certain discrepancies. In the fixed specimen the thrombus appeared to stop just short of the mouths of the superior cerebellar arteries, and it seems safe to infer that they must have remained functionally patent since there was no infarction of any portion of the cerebellum. On the other hand, there must have been at least partial occlusion of the little branches to the midbrain, since sizable areas of infarction were found in this region, as shown by the crosshatched areas in the upper cross-section diagram. There was, of course, extensive infarction of the pontine region, since the mouths of all the pontine branches were covered by the thrombus. This is shown in the middle cross-section diagram.

Judging from the clinical evidence we should have found infarction in the medulla as well, but neither grossly nor microscopically could this be demonstrated. It is possible, of course, that our sections were taken from too low a level.

DR. KUBIK: I suppose it is possible, also, that the symptoms from that area represented a pseudo-bulbar palsy owing to involvement of corticobulbar fibers at a higher level.

DR. MALLORY: The cause of the thrombosis was, I am sure, the usual one—arteriosclerosis. The basilar artery was sclerotic out of proportion to the condition of the other cerebral vessels. All the various communicating vessels of the circle of Willis were in excellent condition.

There was little of interest in the rest of the organs. The lungs showed the congestion and edema characteristic of a cerebral death. There was a slight fibrinous pericarditis, which was sterile, and we were unable to explain it. The endocardium was negative, and there was no obvious source for an embolus.

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THE POSTCONCUSSIONAL SYNDROME

ELSEWHERE in this issue of the *Journal* there is an article on the subject, "The Sequelae of War Head Injuries," concluded from the previous issue. The author, Dr Derek Denny Brown, is the recently appointed professor of neurology at Harvard Medical School and holder of a captaincy in the Royal Army Medical Corps Reserve. As he points out, the work was undertaken with the sponsorship of the Directors General of the Army and Air Force medical services and was actually carried out at Oxford, England. Dr Denny Brown was in charge of the medical division of the hospital that received casualties from both the above organizations. The importance of this work can scarcely be overestimated, and this country, and more es-

pecially the medical departments of the United States Army and Navy, can learn much from it besides the information that is written in the text. For his services in connection with this study Dr Denny Brown received the decoration of OBE from the British Government.

In general the paper presents the English and Continental viewpoint concerning craniocerebral injuries, which differs in certain minor points from the American. For example, the neurosurgeons of this country are prone to be somewhat more practical in their approach; they have, perhaps, a somewhat wider conception of consciousness and the loss of it,* and lean rather more heavily on the accepted pathological definitions. They are, however, still badly befogged about an approach to the problem of the postconcussional or post-traumatic syndrome, and in spite of a different approach, this study can be made to serve as a very useful proving ground for the solution of the dilemma. To be sure, the results cannot be expected to apply exactly to similar industrial accident problems, because Dr Denny Brown did his work among men under discipline, all of whom, it is to be presumed, understood and spoke English and all of whom certainly had an emotional and psychologic approach and reaction to their disabilities that of necessity differed from those of civilians. These are unimportant differences, however, and are mentioned only to emphasize the wide applicability and fundamentality of his new and logical method of approach to this problem. He has finally provided a framework on which to hang in proper order the different psychologic, physical and emotional factors that go to make up the confused whole. With this, he has also emphasized — probably for the first time — the importance of knowing the pretraumatic state under these various categories as an essential to the understanding and proper recognition of the posttraumatic manifestations.

As implied above, another lesson can be learned from the report of this study. It is not included

*Cobl S. *Foundations of the psychosomatics* 1931 p. 50. See also Baltimore: Williams and Wilkins Co., 1941.

in the text but is implicit in the work as a whole. To collect sufficient material, to control its disposition during and after hospitalization and to achieve such results the patients on whom the work was carried out were concentrated in one hospital, which was "a combined services hospital for head injuries." In other words, all patients with cranio-cerebral injuries were taken to a hospital given over to the care of such cases and staffed by specialists in the appropriate line. This segregation of patients with a special type of injury has been practiced for some time in England, and such a scheme implies that appropriately trained surgeons and specialists are also segregated, not only for the benefit of the patients themselves, but also for the advancement of the science of medicine. Among such specialties, neurosurgery holds first place, and it is suggested that the Surgeons General of the United States Army and Navy go and do likewise. The plan would require little if any further dislocation of medical manpower, because many adequately trained neurosurgeons are already in service and are either doing nothing or practicing a specialty other than their own. Now is the time to prepare all over the country for proper care of the wounded in accordance with the special requirements of the wound. Valuable redeemable manpower should not be sacrificed for lack of a little foresight and of mental and organizational initiative.

INSTRUCTION CONCERNING THE TREATMENT OF GAS CASUALTIES

THE Medical Division of the Massachusetts Committee on Public Safety has arranged for state-wide instruction concerning gas warfare. As stated elsewhere in this issue of the *Journal*, the program will be given in each of the nine regional districts of Massachusetts by one of the three teams organized by Boston University, Harvard and Tufts medical schools.

The "course" will consist of a six-hour series of talks covering various aspects of chemical warfare, such as the chemistry of war gases, the action

of the lung-irritating gases and the vesicants, together with the diagnosis and treatment of lesions produced by them, organizational setups for medical decontamination, and group and individual means of protection.

Although protective measures, the identification of the gas used in a raid and the subsequent decontamination of buildings, streets and so forth are the functions of the Protection Division of the Massachusetts Committee on Public Safety, the treatment of gas casualties is solely the responsibility of the Medical Division, and all its members should become thoroughly familiar with the details of therapy. Chief and deputy regional directors, chief and deputy medical officers and physicians attached to medical first-aid posts are urged to attend the course and to pass on the knowledge thus gained to the personnel of their organizations.

MEDICAL EPONYM

SIBSON'S GROOVE

Francis Sibson (1814-1876), while resident surgeon and apothecary to the Nottingham General Hospital, published a paper, entitled "On the External Signs of the Position of the Lungs and Heart," in the *London Medical Gazette* (6:754-760, 1848). A portion of the article follows:

In the healthy robust man the well-formed chest has certain prominences and depressions indicating the organs underneath. . . . A depression crosses the seventh and sixth costal cartilages from the lower end of the sternum to the fifth intercostal space. These depressions are just below the thoracic prominences the right depression exactly indicates the lower margin of the right lung, while the left depression indicates the lower boundary of the heart.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941 (Concluded)

There were 18 cases attributed to embolism that were associated with normal delivery. The first of these was that of a patient who entered a hospital with a temperature of 104°F., x-ray films of the

chest being negative. The second day after entry, pain developed in the right popliteal space; labor began shortly, and she was delivered normally; but death occurred suddenly several hours after delivery. Autopsy showed multiple pulmonary emboli.

The second patient had a normal spontaneous delivery five minutes after hospital entry. Four days later a septic temperature developed and sulfonamide therapy was instituted. This was apparently successful, for the patient was discharged nine days after delivery, the highest temperature for the two days before having been 99°F. One week later she returned to the hospital complaining of pain in the abdomen, and the following day her temperature rose to 104°F. Transfusions were given and sulfonamide therapy repeated; pelvic examination suggested a pelvic phlebitis. Death was sudden, and a diagnosis of septic emboli was made by x-ray examination.

The third case was that of a patient who was not hospitalized, sudden death occurring a month after delivery. The medical examiner made a diagnosis of pulmonary embolism, although no autopsy was performed. It was known that the patient had phlebitis of the left leg.

The fourth patient was an elderly primipara who developed a temperature of 100°F. on the fifth post-partum day, after which mild phlebitis of the left leg developed. The temperature never exceeded 99°F. during her hospital stay. She was allowed out of bed on the ninth day after delivery and complained of severe pain in the right leg. She was allowed up again, however, on the following day, and was about to be discharged when she suddenly collapsed and died. This case was not intelligently handled, and it is quite possible that surgical consultation at the first sign of phlebitis would have resulted in venous ligation and the prevention of this catastrophe.

The fifth patient was delivered spontaneously after a normal labor and had an uneventful convalescence. She was discharged from the hospital at her own request nine days post partum but collapsed shortly after reaching home and died while being conveyed back to the hospital. Although there is no history of phlebitis it may have existed.

The sixth case was that of a patient who had previously had two erythroblastic babies, associated with mild toxemia. The third pregnancy was complicated by increased blood pressure, and albuminuria appearing at about the thirty-fifth week. After six days in a hospital the membranes were artificially ruptured, and normal delivery of an erythroblastic infant, weighing 6 pounds, 9 ounces followed. Convalescence was normal until the sixth post-partum day, when sudden death occurred following an acute pain in the chest.

The seventh patient had an uneventful convalescence following a normal delivery until the seventh post-partum day, when her temperature rose and continued septic for two weeks. Sulfathiazole eventually resulted in subsidence of the fever. While "sitting up in bed and talking" the patient fell back and died within three minutes. The embolus probably originated in the pelvis.

The eighth patient was allowed out of bed ten days following a normal delivery, her convalescence having been uneventful. Death occurred almost instantaneously.

The ninth case was that of a patient who, after a normal delivery and an afebrile convalescence, had a sudden pain in the chest while walking about on the ninth post-partum day; she died within a few minutes. In view of the fact that there was no evidence of phlebitis, it is possible that the embolus arose from the pelvic veins. It is hard to see how such a catastrophe could have been averted if the report of the case is accurate.

The tenth patient went home against advice ten days post partum, having had a slight fever during convalescence. On getting up the following morning, she died suddenly.

The eleventh patient had a convalescence that was complicated by a temperature of 100°F. on the seventh and eighth post-partum days, when pain in the left chest was noted. The temperature was normal during the rest of her hospital stay, and she was discharged a week later. Four days later a phlebitis developed and she was put to bed, but death occurred while she was sitting up in bed drinking a glassful of water. This case again emphasizes the advantage of surgery in certain types of phlebitis.

The twelfth patient, following a normal delivery, had an uneventful convalescence until the eighth day post partum, at which time the temperature ranged from 99.6 to 100.6°F., the slight fever continued until death, which occurred suddenly seventeen days after delivery. During this time there was clinical evidence of a phlebitis, which was treated conservatively by the use of ice. In this case, also, surgical intervention might have been advantageous.

The histories of the remaining 6 cases are inadequate. One record was never received because the patient's family and doctor had moved away and could not be located. The death certificate, however, attributes the death to albuminuria and puerperal embolism. The other 5 patients were delivered normally, one prematurely at seven months. In 4 cases, death occurred almost immediately after delivery, and one of these patients had a massive collapse of the lungs. In the fifth

the lesions, either progressive or regressive, and positive sputum.

Twelve of the patients with positive sputums were over fifty years of age. None of these had marked symptoms at the time the tubercle bacilli were discovered, and some have remained symptom free during two years of observation. In such cases, reactivation may await some new strain, such as an extra physical load imposed on the worker who enters war industry. This is a risk for the healed or arrested case as well.

It is not known whether the higher incidence of tuberculosis in the elderly which we have encountered in a group of unemployed also occurs in elderly persons of higher income levels. Since mortality tables are prepared from deaths at all strata, it would seem possible that this may be the actual state of affairs. In any event, it is of the utmost importance to devote a greater portion of our efforts in tuberculosis case-finding to the discovery of the elderly individual with tuberculosis. This should be done without lessening case-finding measures in young persons, as the latter comprise a larger proportion of the population. Consequently, although the percentage of tuberculosis may be less in those of younger years, the absolute number of cases undoubtedly is greater.

More emphasis should be placed on the examination of all possible sources of a newly diagnosed case of tuberculosis. Even when the older members of a tuberculous household appear to be in the best of health, they should be x-rayed. When a thorough search of the immediate family of an affected person fails to reveal the source of infection, further inquiries should be made as to the identity of others with whom he has most frequent contact, and examination of these persons should be arranged.

The physician should also always suspect tuberculosis in all his elderly patients who have even mild pulmonary symptoms, and should take the necessary steps to rule out this disease before making a final diagnosis.

The most productive method of case finding among the elderly would seem to be the x-ray survey of such population groups. The survey detailed in this paper serves to illustrate the value of such a procedure. Similar surveys concentrated on the older fraction of the population, particularly males, would, we believe, disclose many unknown spreaders of tuberculosis who have been acting as reservoirs of disease in their communities. — Reprinted, in part, from *Tuberculosis Abstracts*, November, 1942.

REPORT OF MEETING

NEW ENGLAND PATHOLOGICAL SOCIETY

A regular meeting of the New England Pathological Society was held on March 19, 1942, at the Peter Bent Brigham Hospital. The program was presented by the Department of Legal Medicine of the Harvard Medical School.

The first paper, "The Law and the Pathologist," was presented by Dr. Hubert W. Smith. He said that, around 1300, the law school at Bologna induced doctors to open dead bodies to determine the cause of death in medico-legal cases. Law was thus father of forensic pathology and the grandsire of orthodox pathology, which subsequently applied like methods to study of disease.

At common law no right of property is recognized in dead bodies, but the surviving spouse, or secondarily the next of kin, has a right to possession of the body, intact as at death, for burial. An unauthorized autopsy invades this right and makes a pathologist liable in damages for mental anguish caused thereby, and jury awards tend to be substantial. Without statute, no privilege exists to perform unconsented autopsies to complete death certificates. Oral or written consent suffices, but as in surgical operations, reasonable mistake does not protect if actual consent is wanting. Conditions can be imposed on consent. Bare consent to autopsy impliedly authorizes retention of microscopic sections but not of gross organs. Jurisdiction of coroners to order autopsy exists only if criminal causation of death is reasonably suspected; orders to aid insurance investigations are void and do not protect the pathologist. Accident policies usually require that the insurer have notice and opportunity to attend autopsies, the beneficiary's innocent violation may forfeit the insurance. Whether a person can authorize an autopsy on himself by contract or will is still controversial. To protect himself here the pathologist should require consent of the next of kin or his employer's agreement for indemnification.

Liability for negligent diagnosis may arise from negligence in identifying the disease or in assuming to diagnose on an improper preparation or specimen.

Pathologists who supervise production of biologic materials may risk liability for injury to remote users due to negligent contamination in manufacture. To prove due care, Dr. Smith advised that aseptic techniques be used, that proper cross-checks and contamination tests be done on random samples, making certain that samples of large batches are retained under sterile conditions to show the product was pure when distributed, that proper labels be used, that known risks inherent in the product be adequately disclosed and that full records covering production and distribution be kept.

The second paper, "Changes in the Magnesium and Chloride Content of the Blood following Drowning in Fresh and Sea Water," was presented by Drs. Walter W. Jetter and Alan R. Moritz. Because the pathological findings after death from drowning are so frequently inconclusive, opinions regarding the cause of death of persons whose bodies have been recovered from water are usually based on negative rather than positive evidence. It has long been known that the electrolyte content of the heart's blood of drowned persons may be altered, and it has been suggested that such changes are pathognomonic of death by drowning. The extent to which the electrolyte concentration in post-mortem samples of blood may show change as a result of causes other than drowning has not been investigated, and experiments were undertaken to determine the significance of such changes in relation to drowning.

Changes in the concentration and distribution of chlorides and magnesium were studied in four groups of dogs. In the first, the animals were sacrificed by mechanically induced asphyxia (not drowning) and allowed to remain in the open air for as long as seventy-two hours after death. The rate of post-mortem change in these animals was regulated by keeping their bodies at different temperatures. In the second group, the animals were sacrificed by mechanical asphyxia and were then submerged in either fresh or sea water throughout the period of post-mortem observation. In the third group, the animals were drowned in fresh water; and in the fourth, they were drowned in sea water. Blood was withdrawn from

the right and left sides of the heart at intervals after death, and the chloride and the magnesium content of both cells and plasma were observed.

In the control animals, it was found that diffusion of both chlorides and magnesium between cells and plasma began soon after death and that within twelve hours the normal ante mortem differences in their concentrations in cells and plasma had usually almost entirely disappeared. The chloride content of heart's blood underwent progressive reduction during putrefaction, whereas the magnesium content became progressively higher. Submersion after death did not alter the rate or character of these changes.

In animals dead of drowning in fresh water there was a sharp drop in the chloride content of the blood in both sides of the heart during the agonal period. The reduction was greater than that observed in any of the control animals. The reduction was more pronounced in the left than in the right side. The difference between the concentrations in the two sides of the heart diminished as putrefaction progressed. Marked hemolysis of left ventricular blood was observed within fifteen minutes after death.

In animals dead of drowning in sea water it was observed almost immediately after death that both the magnesium and the chlorides in the heart's blood were elevated, the former proportionately more than the latter. The elevation was more pronounced in the left than in the right side of the heart. Hemolysis of blood was delayed, and the magnesium content of the stomach was abnormally high.

In the discussion Dr. Moritz stated that he had applied the results of these experimental animals in several cases in human drownings, and that he had found these data distinctly useful.

The third paper, "Adaptive Intimal Changes Which Occur in Arteries following Localized Circulatory Stasis," was presented by Dr. Alan R. Moritz. Varying degrees of local stasis were induced in segments of carotid, brachial and femoral arteries of dogs by means of clamps and ligatures. The degree of stasis varied from complete isolation of unbranched segments of vessels by ligation and section to the application of a single partially obstructive clamp. Segments of arteries were excised for histologic examination at intervals ranging from a few days to a year after operation. Several types of reactive change were observed. Thrombosis occurred in the segments in which the flow of blood had been completely obstructed. In some dogs the thrombi organized and remained completely occlusive, and in others the thrombi became canalized and the obstructions were bypassed. In arteries that had been severely but incompletely obstructed, thrombosis occurred near the sites of ligation or clamping, and intimal proliferation not accompanied by thrombosis produced permanent narrowing of the central portion of the segment in which relative circulatory stasis persisted. In segments of arteries in which the reduction of blood flow was not sufficiently severe to result in thrombosis, two types of reaction were observed. In some the lumen of the affected segment became and remained narrowed by contraction without significant alteration of the intima. In others such functional adaptation to reduced blood flow was accompanied by reactive intimal proliferation. New elastic fibers formed in the hyperplastic intima, and the changes in these vessels were in many respects similar to those that occur in the umbilical arteries of young infants in the first few months after birth, in the uterine arteries of young women during the post partum period, in the arteries of the ovarian cortex during the catamenial

period of life, in the intermediate and small arteries of the kidneys of persons suffering from certain forms of chronic Bright's disease and the splenic arteries of infants and children following splenectomy.

The results of this study suggest that certain of the arterial and arteriolar lesions heretofore regarded as primary may actually represent a secondary adaptive reaction to reduced blood flow incident to destructive or involutional parenchymatous change.

In the discussion Dr. B. E. Clarke asked, if all these changes are adaptive, how Dr. Moritz explained changes in the placenta during pregnancy where there is a similar process taking place, although the placenta is growing. Dr. Moritz stated that he did not know but that he did not believe that the changes in the uterine and ovarian arteries are entirely adaptive.

In answer to Dr. M. J. Schlesinger's question whether this adaptive change is better in young people because of the abundance of new smooth muscle and elastic tissue that is being laid down, the speaker replied that there is no age relation, so far as the dog is concerned. In human beings, however, the best changes were seen in the splenic arteries following splenectomy. The vessels of young people are best because they are likeliest to have no pre-existing intimal change.

The fourth paper, "Medicolegal Tests for the Identification of Seminal Fluid," was presented by Dr. O. J. Pollak. The evaluation of tests for semen is based on the definition of rape by law. Recovery of semen presents supporting evidence, together with genital, perigenital and remote injuries on the person of the victim and the suspect.

Male ejaculate may be found in the female genitals, on the body or on objects. Motile spermatozoa may be detected in the vagina up to three hours, in the cervix up to one hundred hours, and immobilized spermatozoa in the vagina up to twenty-four hours and in the cervix up to seven and a half days after intercourse. No conclusions are allowed as to the time elapsed after copulation or after death.

Outside the genitals, semen dries and often is absorbed by the soiled material. Stains are detected by ultraviolet rays of chemical indicators. From fresh material, films are made and stained with Giemsa's stain. Findings are tabulated in a spermogram and so biometric curves. If the material is dried, complete mechanical destruction by teasing the fabric into finest shreds and subsequent staining, or chemical decomposition in concentrated sulfuric acid and examination of the residue are the two ways leading to the recovery of spermatozoa. Positive findings in fabric boiled in water for twenty minutes demonstrate that spermatozoa firmly adhere to the support. This explains the failure of other methods.

If no spermatozoa can be found, immunological methods may reveal the true nature of a stain. The often recommended microchemical tests are neither sensitive nor specific. Material is differentiated from animal substrate and identified as semen by precipitin tests performed with antihuman semen serum after absorption with human blood. Grouping of semen and semen stains with the absorption technique is invaluable for establishing semen individuality provided that it is carried out under proper controls and with criticism.

In the discussion Dr. Moritz emphasized the point that, from a medicolegal standpoint, by far the most valuable scientific evidence is provided by the demonstration of the spermatozoa and added that all methods should be tried to demonstrate the spermatozoa before

resorting to the immunologic method, which is a complicated procedure. The average juror is happier if shown a photograph of the spermatozoa than if confronted with complicated tests that require the immunization of animals.

The fifth paper, "An Experimental Investigation of the Stability and Distribution of Carboxyl Hemoglobin after Death, with Particular Reference to the Difficulties Sometimes Encountered in Incinerated Bodies," was presented by Dr. Herbert S. Breyfogle. Attention was called to three problems incident to medicolegal investigation of suspected carbon monoxide inhalation. First, the presence of carbon monoxide in burned bodies is important in the proof that a person was alive when exposed to flames. Burning, however, may reduce the blood to a solid coagulum, presenting a technical difficulty in the detection of carbon monoxide; however, a qualitative method was described for the detection of carbon monoxide hemochromogen in such blood, which also permits the recovery gasometrically of small amounts. Secondly, the presence of carbon monoxide in extravasations of blood resulting from injury is important in determining whether an injury preceded or followed inhalation of carbon monoxide. Cases were cited showing the value of this information, and experimental studies were presented indicating that carbon monoxide-free hemorrhagic extravasations do not take up the gas from circulating blood rich in carbon monoxide and that post-mortem diffusion of carbon monoxide following fatal asphyxia by this agent does not occur. Finally, the relation of carbon monoxide and putrefaction was discussed. Various claims made in the literature indicate that carbon monoxide may be demonstrated for as long as twenty months after death, regardless of the state of the cadaver; however, in dogs asphyxiated with carbon monoxide and left at room temperature up to seventy-two hours there was a gradual decline in the saturation of carbon monoxide amounting to 5 per cent every twenty-four hours. Control studies indicated that carbon monoxide is not ordinarily generated incident to the putrefaction of animal tissue.

In the discussion Dr. W. J. Brickley stated that if the buried body has already been embalmed, it is best to examine blood from the iliac arteries for carbon monoxide because usually the embalming fluid does not reach these arteries so easily. Dr. Clarke reported that he had studied the blood removed from 24 people who had been found in burned houses, and in three cases in which no carbon monoxide was found, it was discovered that a deliberative attempt had been made to dispose of the body by burning. Two men had been shot, and the third had been hit over the head. All the rest showed a relatively high carbon monoxide content. This matter is of considerable practical importance in the investigation of bodies found in basements of burned houses.

In closing the speaker stated that if embalming does take place immediately post mortem, some blood may be preserved.

The last paper, presented by Dr. J. C. Bequaert, was entitled, "Some Observations on the Fauna of Putrefaction and Its Potential Value in Establishing the Time of Death." On animal and human corpses, from the time of death until the final disintegration of all tissues, except the bones, there is a definite and orderly succession of arthropods (insects and mites) feeding on the tissues. Each species arrives at a certain stage of decay, to be replaced by one or more others at the next stage. The duration of each stage and the species of arthropods present vary with the nature of the dead body, the climate, the sea-

sons, the condition of exposure or burial, the locality (whether city or country) and the region of the earth. All these factors must be properly studied before reliable medicolegal conclusions can be drawn from some particular arthropod found on a corpse. Few such studies have been made thus far, the most complete to date being those of Megnin in Central France. This investigator recognized on a human corpse left in the open eight types or "squads" of necrophagous arthropods succeeding one another at the following eight stages of decay: fresh or recent corpse; early putrefaction; butyric fermentation; caseic fermentation; ammoniacal fermentation; mummification of tissues; removal of dried tissues and hairs; and skeleton. As each of these stages lasts a certain time, Megnin claimed to be able to deduce the time elapsed since death occurred from the species of arthropods found with the corpse when it was discovered. He described a number of cases in which his method was applied and pointed out that in some of them confessions by the criminals involved proved that he was correct. In America, Johnston and Villeneuve (1897) investigated the fauna of freely exposed cadavers in southern Quebec; and Motter (1898) studied the arthropods found after exhumation. From 1894 to 1897, the late Dr. Garry deN. Hough, of New Bedford, did considerable research on the fauna of dead bodies, but his findings were never published. Dr. Bequaert concluded with a discussion of the arthropods found on two corpses discovered in the open in Massachusetts.

BOOK REVIEW

Science and Sanity: An introduction to non-Aristotelian systems and general semantics. By Alfred Korzybski. Second edition, with a supplementary introduction and bibliography. 8°, paper, 842 pp., with 95 illustrations. Lancaster, Pennsylvania: The International Non-Aristotelian Library Publishing Company, 1941. \$6.00.

The second edition of this suggestive and most provocative book will make a serious appeal to those who deal, or wish to deal, with the psychologic reactions of a given person to words and language and other symbols and events in connection with their meanings. "Meaning" for this author must be considered as a multidimensional term as it applies to all levels of abstraction; the concept of multidimensionality is inherent in the structure of "human knowledge." The main thesis of the book revolves about the concept that the Aristotelian "laws of thought" formulated as the law of identity, the law of contradiction and the law of the excluded middle, were satisfactory for an earlier epoch but are no longer productive of sanity for these times. What is needed is a new non-Aristotelian system completely free of these laws.

The author builds an interesting diagram of a "structural differential" necessary for one to receive full semantic benefit, since if one is to differentiate he cannot identify. The argument is forcibly presented that to achieve sanity one must study the structural characteristics of this world first, as scientists do, and only later build languages of similar structure. Illustrations are drawn from the fields of mathematics, physics and biology to support the author's thesis. The book is not easy to read, but when one has once done so, it will surely lead to a second reading and increased profit. The first appearance of this book stimulated the establishment of courses covering the topic in certain universities.

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HEMOLYTIC TRANSFUSION REACTIONS DUE TO THE Rh FACTOR: A PREVENTABLE DANGER*

LOUIS K. DIAMOND, M.D.†

BOSTON

WITH the modern technic of grouping and cross-matching the bloods of donors and recipients, hemolytic transfusion reactions due to incompatibilities involving the A and B agglutinogens are exceedingly rare. In an analysis of more than 3000 transfusions Wiener et al.¹ found only two such reactions due to gross incompatibility. However, the occurrence of hemolytic transfusion reactions in spite of the use of blood of the proper group—that is, due to intragroup incompatibilities—has recently aroused much interest. An important step toward eliminating such hemolytic reactions and preventing serious if not fatal kidney insufficiency from transfusion of incompatible blood has been the discovery of the Rh agglutino-gen of human red blood cells and the modes of development of an anti-Rh agglutinin in the serum of persons lacking this red-cell factor.

In 1939, Levine and Stetson² reported an unusual case of intragroup incompatibility and first called attention to the role of the fetus in causing isoimmunization in a pregnant woman. In 1940, Landsteiner and Wiener³ described an agglutinable factor in human blood demonstrable by immune serums produced against the red cells of the Indian macaque (*Macaca rhesus*). This agglutino-gen, called the "Rh (rhesus) factor," was later proved by the same workers⁴ to be present in the red cells of about 85 per cent of the white population (Rh+ persons) and absent in about 15 per cent (Rh- persons).

In 1940, Wiener and Peters⁵ described hemolytic reactions following transfusions of blood of a homologous group. In 3 cases the Rh factor was involved. Also in 1940, Levine and Katzin⁶ described the varieties of isoagglutinins that may result from isoimmunization in pregnancy, and pointed out that the specificity of one serum con-

taining "warm" agglutinins corresponded to the anti-Rh agglutinins of Landsteiner and Wiener.³ The following year, Wiener⁷ published further observations on hemolytic reactions involving the Rh factor, with and without demonstrable antibodies.

In a timely warning, Levine⁸ stressed the frequency of transfusion accidents in pregnant women, stating that the Rh factor was the antigenic agent in the great majority of cases. He also pointed out that a modified compatibility test might aid in the detection of incompatibilities. For this test, a mixture of donor's cells and recipient's serum in a test tube is incubated at 37°C. for a half to one hour, centrifuged for one minute and examined for agglutination.

By these and further steps, Levine and his associates⁹ and Wiener demonstrated the importance of the Rh factor and of the development of anti-Rh agglutinins in recipients as the cause of previously baffling intragroup transfusion reactions.

Since these pioneer investigations, there have been a number of case reports of reactions involving the Rh factor and anti-Rh agglutinins.¹⁰⁻¹³

An important corollary of the investigations by Levine and his associates^{14, 15} of the presence of an anti-Rh agglutinin in the serums of pregnant women suffering intragroup transfusion accidents was their discovery of the role of the anti-Rh antibody in the pathogenesis of erythroblastosis foetalis in the offspring. The presence of an Rh+ fetus (this blood factor being inherited from the father as a dominant characteristic) in an Rh- woman may, in a small number of matings, permit the passage of Rh+ blood cells into the maternal circulation, with resultant isoimmunization and the development of an anti-Rh agglutinin. This, being a soluble component of the serum, enters the fetal circulation. When present in sufficient concentration over a period of months, the anti-Rh agglutinin, acting on the Rh+ cells of the infant, may cause jaundice, anemia, overproduction of nucle-

*From the Department of Pediatrics, Harvard Medical School, the Children's Hospital, and the Blood Grouping Laboratory, Boston.

†Assistant professor of pediatrics, Harvard Medical School, visiting physician, Children's Hospital.

ated red cells and all the other signs and symptoms of the condition known as erythroblastosis foetalis.

Transfusion reactions occurring in 10 cases serve as the basis for this report. In every case the recipient was found to have received blood compatible according to tests for the blood groups, but incompatible with regard to the Rh factor; that is, the donor's blood was Rh+, whereas the recipient lacked the Rh factor and had had a means of isoimmunization previously, leading to the development of an anti-Rh agglutinin. In another patient (Case 11), an anti-Rh agglutinin was demonstrated early and a transfusion reaction was avoided.

METHOD OF TESTING

The method of testing for the Rh factor, as described by Levine et al.,¹⁵ consists of making a 2 per cent (roughly) suspension of the unknown erythrocytes in normal saline solution, placing 2 drops of this suspension in a 7-mm. test tube (Kahn type), adding 1 or 2 drops of the neutralized* anti-Rh serum, incubating for about 1 hour in a water bath, at 37°C., centrifuging at about 500 revolutions for 1 minute and then by gentle agitation resuspending the cell button formed on the bottom of the tube. Gross clumping is visible to the naked eye or, if the clumps are smaller, through a hand lens. The doubtful and apparently negative reactions are checked by examination of a drop placed on a slide under the microscope. Landsteiner⁴ has advised judging the positive reactions by examination of the cell button for smoothness or irregularity, but for the inexperienced observer the microscopic examination seems easier. Rh+ cells often are clumped at the end of 15 minutes or less of incubation. If haste is essential, the test can be set up in duplicate and placed in the warming bath. At the end of 15 minutes, one tube is centrifuged and the test read. If negative at this time the incubation of the other tube is continued for the full hour, before a final reading is made.

Since according to Levine[†] the Rh factor is a complex antigen, and the human serums used for typing are the result of specific immunization with one or another Rh+ cell, it is necessary to know beforehand how specific the testing serum is, and in many cases to use more than one anti-Rh serum. As a rule, at least two serums are used, one which yields about 70 per cent positive reactions, and the other about 87 per cent. To date, serums produced experimentally in laboratory animals have not been satisfactory or available, and only human serums have therefore been used. Only a small percentage of Rh-human beings, when immunized by transfusions of Rh+ blood or by pregnancies involving a fetus having the Rh factor, develop anti-Rh agglutinins. Often these give weak reactions in vitro, even though the in-vivo reactions may be marked, and the titer if high remains so for only a short time after the transfusion reactions or the termination of the pregnancy that stimulated the isoimmunization. For these reasons, sources of anti-Rh serums of high titer are difficult to find.

*Neutralized with Witelsky soluble A and B factors, obtained through the courtesy of Dr. Witelsky and the Eli Lilly Company, Indianapolis.
†Personal communication.

In testing an unknown serum for the anti-Rh agglutinin, it is advisable to use known Rh+ cells from different persons, choosing Group O erythrocytes or those of the same group as the unknown whose serum is being tested. To avoid missing a weak agglutinin or obtaining questionable readings and to determine the specificity of the anti-Rh serum when it is present, it has been found best to use at least ten samples of Rh+ cells, each of a different antigenic composition. The mixtures of cells and serum are incubated, centrifuged and read as described above.

CASE REPORTS[‡]

CASE 1. A 45-year-old man with aplastic anemia had received four transfusions of compatible blood 5 months previous to admission, without a serious reaction. At the present entry a Group O donor was used, who by the usual cross-matching technic was apparently compatible. A moderate reaction to this transfusion resulted, with pain in the flanks, mild hemoglobinuria, fever and jaundice and with no apparent improvement in the anemia. A second transfusion, immediately following the first, produced a severer reaction.

Re-examination of the patient's and the donor's blood samples, taken within a few hours after the last reaction, showed each to be Group O. The donor's cells were strongly Rh+. A test of the recipient's cells with anti-Rh serum produced gross clumping. However, microscopically the clumps were large but rare and most of the cells were unagglutinated. It seemed probable, therefore, that the recipient's blood contained a mixture of Rh+ (donor's) and Rh- (recipient's) cells. Test of the patient's serum showed no anti-Rh agglutinin at this time.

Two transfusions of Rh- blood were given, with no reaction and with a satisfactory rise in the erythrocyte and hemoglobin values. Another test of the patient's serum, 11 days after the reaction, showed slight but definite clumping of Rh+ cells.

Ten more transfusions of Rh- blood were given in the following 4 months, with no untoward effects.

CASE 2. A 30-year-old man with massive hemorrhage from a duodenal ulcer was given multiple transfusions. At the end of the fourth transfusion, a slight febrile reaction was noted. The fifth transfusion was followed by a severe reaction and evidences of hemolysis.

Blood from the last donor and from the recipient taken 2 hours after this reaction showed the donor's cells to be Group O and Rh+, and the patient's cells likewise Group O, with some gross clumping in the anti-Rh serum. Microscopically the majority of the cells were single, there being only a few large clumps. This suggested a mixture of Rh+ and Rh- cells. Tests for the anti-Rh agglutinin in the patient's serum were negative at this time. A transfusion of Rh- blood was given, with a satisfactory response.

Retesting of the patient's blood 11 days after the reaction showed the red cells to be definitely Rh-. The serum failed to agglutinate any of ten different Rh+ cell samples.

CASE 3. A 12-year-old girl with profound anemia from bleeding intestinal polyps was given two transfusions, with

[‡]Cases 1, 2, 3, 5 and 6 are from the files of the Blood Grouping Laboratory, an organization formed by the Boston Lying-in Hospital, the Massachusetts Memorial Hospitals and the Children's Hospital for the purpose of typing blood for the Rh factor, investigating transfusion reactions and procuring suitable donors on demand.

no untoward reaction. Two weeks later, another transfusion with matched compatible blood was administered but was followed by a severe hemolytic and febrile reaction. A specimen of the first donor's blood and a sample of the patient's blood taken after the reaction were obtained. The donor's cells were Group O and strongly Rh+. The recipient's Group O cells likewise had some clumping grossly, but under microscopic examination the clumps were scarce though large, and most of the cells were unagglutinated, suggesting the presence of some Rh+ cells in an Rh- person. Further confirmation of this was found by tests for the M and N factors. The donor's blood was Type M, the mixed blood showed both M and N cells, the patient's blood at a later test was Type N and Rh-. Tests for the anti Rh agglutinin in the recipient's serum showed none present in the first sample but a definite trace detectable two weeks later.

Rh- blood was used for a subsequent transfusion, with no untoward reaction.

CASE 4* A 54-year-old woman had had four uncomplicated pregnancies from the ages of 19 to 30. She was known to be suffering from chronic anemia and had received her first transfusion of 600 cc of blood from her husband in April, 1937, with no reaction. In October 1940, a second transfusion of blood from her husband was given but had to be discontinued after only 325 cc had been administered, because of a chill and sudden fever. In December, 1940, a diagnosis of congenital hemolytic jaundice was made for the first time, and on January 4, 1941, in preparation for splenectomy a third transfusion of 500 cc of blood from a friend was given with no reaction. On January 7, the husband was again tried as donor for a fourth transfusion, since ordinary cross-matching showed no incompatibility. After 200 cc of blood had been given, a severe hemolytic reaction occurred, with hemoglobinemia, hemoglobinuria and fever. The next day a friend was used for a fifth transfusion and again, after 300 cc had been received, the patient had a severe hemolytic reaction similar to that of the previous day. The patient was finally subjected to splenectomy on January 31, and during and after operation a sixth transfusion of 500 cc from a friend and a seventh from her brother were given in immediate succession. The latter transfusion had to be halted after 300 cc of blood had been used, owing to a chill and a high temperature, although no hemoglobinuria developed. Despite this, the patient made a fair recovery and has been well since.

Subsequent typing of the patient's and the various donors' bloods revealed that the husband's cells were Group O (M and N factors) and Rh+, whereas the wife's were Group A (M factor) and Rh-. Of the donors, the blood used for the third transfusion, at which time no reaction occurred, was Group O (M and N factors) and Rh-. All the other bloods given were Rh+, and the transfusions were followed by reactions. The first two, from the husband, were presumably the stimuli for sensitization. No anti Rh agglutinin was detected 2 days, 11 days, and 11 months after the hemolytic reactions.

CASE 5 A 5-year-old boy was admitted with the diagnosis of chronic progressive nephritis in a nephrotic crisis.

with marked generalized edema, ascites and a lowered serum protein level. No transfusion had been given previously. In preparation for transfusion the patient's blood was matched against that of two donors, both Group O, as was he. In the cross-matching, the donor's cells showed slight clumping in the recipient's serum but there was no clumping of the patient's cells in the donor's serums or in his own serum. Further studies revealed that both donors were Rh+ and the patient Rh-, and that his blood serum agglutinated seven samples of Rh+ cells but none of Rh- cells. The clumping was present to a slight extent at room temperature, and more definitely after incubation for an hour at 37°C. Accordingly, a transfusion of 300 cc. of blood from an Rh- donor was given. No untoward effect was seen.

During the ensuing 3 months, six transfusions of Rh- blood were given, without reaction.

Cases 6, 7, 8 and 9. These patients were essentially alike in that each was a young multipara (the ages being 22 to 34 years) who had had no previous transfusions but had given birth at a second pregnancy to an infant with erythroblastosis foetalis. A transfusion administered at the time of or shortly after this delivery had been followed by a hemolytic reaction.

Tests on the bloods of the mothers showed that each was Rh-. In every case, the father and the children were Rh+. Anti Rh agglutinins were detected in the serum of each recipient. One or more transfusions with Rh-compatible blood were then given, with no untoward reactions.

CASE 10† A 19-year-old woman was delivered of a stillborn infant, which showed clinically congenital hydrops and pathologically all the criteria of erythroblastosis foetalis. Since such an occurrence in association with a first pregnancy is extremely rare a careful investigation of the patient's past history was made, with the following results. Three and a half years previously, the patient had required repeated transfusions after the removal of a chest tumor. In 2 months six transfusions were given, — the patient and donors being Group O and compatible by cross-matching, — with no unusual reaction. About 2 years later, a thoracoplasty was done and the patient was given four more transfusions in 4 days. The last two of these were followed by moderately severe reactions. The patient made a good recovery, was married before pregnant and delivered the hydropic infant mentioned above.

Tests on the blood of the patient's husband (reported as a donor for her) showed him to be Group O and Rh+. The patient herself was Group O and Rh-. Tests on donors used for her last two transfusions (12 months previous) showed them to be Group O and Rh+. Tests for anti Rh agglutinins were negative.

CASE 11‡ A 41-year-old woman was delivered of a sixth child, which shortly after birth died of erythroblastosis foetalis, with marked edema and jaundice. The obstetric history was most important. Five previous pregnancies had ended in the delivery of stillborn infants who had continued entirely well through the pregnancy had been cesarean section because of fetal distress. The infant had died of fetal distress.

*This case was reported by Dr. H. W. Henshaw, Boston City Hospital, Boston.

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*This case with its interesting and initially baffling transfusion reaction was included in the case reported by Wiener (Case 9). The more complete studies were carried out recently in co-operation with Dr. T. Hale Han of the Thorndike Memorial Laboratory, Boston City Hospital to whom I am indebted for this report.

tion revealed no evidence of erythroblastosis foetalis. After the operation the mother received a transfusion from an apparently compatible donor (later proved to be Rh+) and had no reaction. During the sixth and last pregnancy the patient developed signs of mild eclampsia and went into active labor at the end of the 8th month, with the result mentioned above.

After the delivery, palpation revealed a tear in the muscle of the uterus. Hysterectomy was therefore done. Following this, four successive transfusions of apparently compatible blood were given, each being followed by greater collapse, and then hemoglobinuria, hemoglobine-mia, jaundice and finally almost complete anuria. In the following 10 days, three more transfusions of known Rh-blood were given, with no untoward reactions. Alkalinization therapy and decapsulation of the kidneys were carried out, but the patient succumbed to uremia and terminal infection.

Grouping and typing of the patient's blood after the fourth transfusion showed her to be Group O and Rh-. A strong titer of anti-Rh agglutinin was easily demonstrated in her serum. The husband and two of the children were Group O and Rh+. The first four donors used after the sixth pregnancy were all Group O and Rh+. Their cells were agglutinated by the patient's serum at 37°C. after 1 hour's incubation. The cells of the Rh-donors used subsequently were not agglutinated by the patient's serum.

COMMENT

In Cases 1, 2 and 3, the reactions occurred following the use of Rh+ blood for patients who were lacking the Rh factor and had been immunized by previous transfusions, probably from Rh+ donors. However, the anti-Rh agglutinin was not demonstrable by in-vitro tests on the serums of these patients immediately after the reactions occurred, when it presumably might have been absent because of having been absorbed out by the donor's Rh+ cells or, in one case, even at a later time when it might have reaccumulated. It may be assumed that the titer of this antibody was relatively low in these patients, not only because of the failure to demonstrate agglutination but because the transfusion reactions were not very severe, and especially because donors' cells were still circulating, unagglutinated, in the recipients' blood streams twenty-four hours after the transfusions. This caused some confusion in reading the Rh tests on the patients' bloods at this time, since there were some clumps of cells, suggesting an Rh+ result. But the majority of the cells showed no agglutination with the anti-Rh testing serum, indicating a mixture of a small number of Rh+ cells with a larger amount of Rh- blood. Tests a week or more after the reaction showed only Rh-blood in each recipient, the donor's incompatible Rh+ cells having been destroyed. One or more transfusions from known Rh- donors were given, without untoward reactions. In Case 3, testing for M and N factors confirmed the fact that the

first blood sample after the transfusion reaction contained mixed blood.

Case 4, in which the patient had congenital hemolytic jaundice, is of interest because of the occurrence of five transfusion reactions when the bloods of donors later proved to carry the Rh factor were used. The first transfusion from the patient's husband, whose blood was Rh+, stimulated the isoimmunization that led to the later reactions. The only transfusion other than the first that was tolerated without untoward effect was the third, from a donor later shown to be Rh-. The anti-Rh agglutinin could not have been a strong one, for in three separate tests it was not demonstrable in vitro and the patient survived five injections of incompatible blood, totaling 1625 cc., in four months.

Case 5 is baffling because the patient, a child suffering from chronic nephritis with the nephrotic syndrome, showed an anti-Rh agglutinin without ever having received a transfusion, according to the history, and careful investigation failed to reveal any discrepancy in this story. It raises the interesting possibility of a naturally occurring anti-Rh agglutinin in some persons who lack the Rh factor. Possibly the nephrotic state had some bearing on this, for in Wiener's⁷ Case 8, the patient was an Rh- child with nephrosis who failed to show an increase in the red-cell count even with the first few transfusions of Rh+ blood. This suggests the presence in this patient of an anti-Rh agglutinin that only in subsequent transfusions became sufficiently strong to produce a true transfusion reaction.

The next four patients (Cases 6, 7, 8 and 9) developed anti-Rh agglutinins not as the result of previous transfusion with Rh+ blood but through isoimmunization by the fetus. In each case the father and the children were Rh+, whereas the mother's blood lacked this factor. Although in each family the first child had shown no evidences of erythroblastosis foetalis, — and this is the usual finding, — the second pregnancy had resulted in the birth of an infant with this condition. Levine et al.⁹ have postulated that the first infant usually escapes because one or more pregnancies involving an Rh+ offspring may be necessary to induce a sufficient degree of isoimmunization in the Rh-mother to harm the fetus and produce the symptoms of the disease. In the 4 cases reported here, the anti-Rh agglutinin was easily demonstrable in tests of the serum and thus explained the severe reactions that followed transfusion with Rh+ blood. The use of Rh- blood was regularly successful.

Isoimmunization through pregnancy rather than through previous transfusion alone seems to pro-

ice a higher, more sustained and easily demonstrable titer of anti-Rh agglutinin.* Certainly, reactions even with the first incompatible transfusion in such women tend to be severer or even fatal, whereas in Cases 1, 2, 3 and 4 several incompatible transfusions were given without the development of kidney insufficiency or serious hemolysis.

Case 10 illustrates the damage that may result when an Rh- woman married to an Rh+ man develops isoimmunization as the result of transfusions of Rh+ blood. This patient had eight transfusions, most of them, presumably, from

This, however, was the stimulus to isoimmunization. The next infant developed erythroblastosis foetalis and succumbed shortly after birth. Further transfusion with Rh+ blood resulted in serious reactions, with kidney insufficiency and eventual death.

SUMMARY

Brief case histories of 10 patients who suffered hemolytic transfusion reactions are presented (Table 1). In every case, the recipient received compatible blood according to grouping and cross-matching by the ordinary methods. Later inves-

TABLE 1. *Summary of Data.*[†]

SE No.	SEX	AGE yr.	DIAGNOSIS	MEANS OF ISOIMMUNIZATION	RESULTS OF ANTI RH TESTS
1	M	45	Aplastic anemia	Repeated transfusions	Immediately after reaction, negative 11 days later slight trace
2	M	30	Bleeding (duodenal ulcer)	Repeated transfusions	Immediately after reaction negative, 11 days later negative
3	F	12	Bleeding (intestinal polyps)	Repeated transfusions	Immediately after reaction negative, 2 weeks later, trace
4	F	54	Congenital hemolytic jaundice	Repeated transfusions	Two days 11 days 11 months after reaction, all negative
5	M	5	Chronic nephritis with ascites and edema	Not known (possibly spontaneous isoagglutinin)	At 2 tests, trace
6, 7, 8, 9	F	22-34	Pregnancy with post partum bleeding	Pregnancy with Rh+ fetus	Trace to moderate reactions
10	F	19	Pregnancy following thoracoplasty and hemorrhage	Repeated transfusions, possibly pregnancy with Rh+ fetus	No tests done
11	F	40	Pregnancy with post partum bleeding	Repeated transfusions, possibly pregnancy with Rh+ fetus	Strong titer after fourth reaction

[†]In every case except Case 5 (where an incompatible transfusion was avoided) tests for the Rh factor showed the recipient to be Rh- and the donor's blood producing the reaction to be Rh+, mixed reactions were found in Cases 1, 2 and 3, as described in the case reports.

th+ individuals. The last two were followed by hemolytic reactions. Her first pregnancy resulted in a baby with severe hydrops due to erythroblastosis foetalis. This is a rare if not unique occurrence. It suggests that the mother carried a high titer of anti-Rh agglutinin from early in pregnancy, possibly increased by the presence of the Rh+ fetus, and that this soluble antibody produced severe damage in the infant. This enforces the urgent need for using only Rh- blood for transfusions, especially repeated ones, in Rh- patients, for the protection both of the recipient and—in women—of the potential offspring.

Case 11 offers even more fertile ground for speculation concerning the damage to an Rh- woman and her future children that may result from a transfusion with Rh+ blood. This mother had given birth to four Rh+ children with no stigmas of erythroblastosis foetalis. Thus there was no evidence of isoimmunization, especially since after her fifth pregnancy she was able to tolerate transfusion of Rh+ blood without reaction.

*Levine in personal communications has mentioned repeated observations affirming the belief that better immunizing opportunities are afforded pregnancy than by repeated transfusions.

igation disclosed that the incompatibility involved the Rh factor. Each recipient was Rh-, and through the development of isoimmune bodies to the Rh factor suffered a hemolytic reaction when Rh+ blood was administered.

Isoimmunization occurred in some patients as the result of previous transfusions with Rh+ blood; in others, as the result of a pregnancy involving a fetus having Rh+ blood cells. In still another patient, an anti-Rh agglutinin of natural origin seemed to be present.

Mixtures of recipient's Rh- cells and donor's Rh+ cells were observed in the blood of 3 patients shortly after hemolytic transfusion reactions had occurred. This necessitated care in interpretation of the test for Rh+ cell agglutination. In 2 cases, women of childbearing age developed isoimmunization to the Rh factor through the use of Rh+ blood for transfusions, and in both these cases, this seemed to have been the direct cause of the birth of an infant with severe erythroblastosis foetalis in a subsequent pregnancy.

Following the hemolytic reaction, the use of Rh- blood for subsequent transfusions in each patient resulted in no further difficulties.

CONCLUSIONS

Patients who are likely to have repeated transfusions should be typed for the Rh factor, to avoid immunizing Rh- persons by the use of Rh+ blood. This is especially important in women of childbearing age, to avoid the possibility of harming an Rh+ fetus at a later pregnancy.

Women who may require transfusion during or after pregnancy should be typed for the Rh factor and, if Rh-, receive only similar blood. This is especially important if the obstetrical history suggests the birth of an infant with erythroblastosis foetalis. In the latter event the husband is a dangerous donor.

The modified compatibility test of Levine (incubation of the mixture of donor's cells and patient's serum before examination for agglutination) occasionally reveals the presence of the anti-Rh agglutinin in the recipient's serum. If negative, however, it is not a guarantee that a hemolytic reaction will not occur.

Rh- donors should be listed and be available for transfusion of Rh- patients, or those untyped recipients whose history suggests the possibility of transfusion reactions.

Laboratories should be equipped, at least in the larger medical centers, to carry out typings for the Rh factor, thus helping to procure Rh- donors, to detect anti-Rh agglutinins and to study, and so help to prevent, transfusion reactions.

300 Longwood Avenue

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THE TREATMENT OF CANCER OF THE PROSTATE WITH CASTRATION AND THE ADMINISTRATION OF ESTROGEN*

A Preliminary Report

RICHIARO CHUTE, M.D.,† AND LIEUT. ARTHUR T. WILLETTTS (MC), U.S.N.R.‡

BOSTON

IN THE spring of 1941, Huggins and his co-workers^{1,2} reported a series of cases of carcinoma of the prostate with demonstrable metastases or local extension, the majority of which had been greatly benefited both subjectively and objectively by reducing the physiologic action of the androgens in the body. This had been accomplished either by reducing their production by surgical castration, or by biochemically inactivating or neutralizing the existing androgens by the administration of estrogen or by a combination of the two. In view of the obvious importance of this work, a brief explanation of the principles involved seems indicated.

Huggins attacked the problem of carcinoma of the prostate in various ways, one of which was by investigating its connection with so-called "acid" phosphatase. This enzyme is thus named because it manifests an optimum activity at about pH 5.0, as distinguished from the better-known alkaline phosphatase, whose optimum activity occurs at about pH 9.3 and which is associated with osteoblastic activity in the bones. Before puberty, acid phosphatase is present in prostatic tissue in only small amounts, but after puberty it is found in large amounts in the normal prostate, which is the chief source of acid phosphatase in the body. Furthermore, acid phosphatase is also present in large amounts not only in prostatic carcinoma tissue but also in the tissue of the metastases to bone of this disease. It is also known that acid phosphatase is present in the serum of patients with metastases from carcinoma of the prostate in a far greater concentration than in the serum of normal men or men with prostatic cancer but without metastases.³ This is thought to be due to neoplastic invasion of the lymph or blood channels with escape of the enzyme into the circulating fluids. Thus it is supposed that an elevated serum acid phosphatase signifies cancer of the prostate with metastases, and that a rising level of serum acid phosphatase indicates an increase of metastatic disease, with an unfavorable prognosis. These facts suggested to Huggins the probability that many cases of prostatic carcinoma represent a ma-

lignant overgrowth of adult prostatic epithelial cells, and that therefore the same factors that inhibit the growth of adult prostatic epithelial cells may also inhibit the growth of prostatic carcinoma cells. He knew that prepuberal castration usually prevents the development of the prostate, and he also knew from the clinical reports in the 1890's of White⁴ and of Cabot,⁵ and from his own experimental work,⁶ that surgical castration causes atrophy of adult prostatic epithelial cells. Furthermore, he knew from his own work⁷ and that of others^{8,9} that the administration of estrogen did the same thing. Therefore, he tried surgical castration or estrogen administration, or a combination of the two, on more than 20 cases of carcinoma of the prostate, using the behavior of serum acid phosphatase, in those cases where it was elevated owing to metastases, as one of the yardsticks of the amount of activity of the prostatic carcinoma cells and of their response to any inhibiting influence. He found that this type of therapy reduced an elevated serum acid phosphatase practically to normal, and therefore presumably greatly reduced the activity of the prostatic carcinoma cells. Another evidence of reduction of this activity, and a result obviously of the utmost clinical significance, was the occurrence of a great diminution in the size and induration of the carcinomatous prostate itself. In addition, metastatic pains were greatly relieved, and the general condition of the patient improved markedly.

These favorable results reported by Huggins in about 80 per cent of his series of more than 20 consecutive patients, some of whom had been followed for more than two years, were so promising in the treatment of this particularly difficult and distressing disease that we were prompted to try this type of treatment at the Massachusetts General Hospital. This paper deals with the results obtained in 37 patients with carcinoma of the prostate treated from July, 1941, to July, 1942. Although at the time of writing nearly 50 cases have been so treated, the follow-up period on the later cases has been so short that it seems more suitable to present the results only in the 37 cases treated during the first year. A year is, of course, too short a time in which to be able to appraise the final value of the treatment, but since

*From the Urological Service of the Massachusetts General Hospital.

†Assistant in genitourinary surgery, Harvard Medical School; associate urologist, Massachusetts General Hospital.

‡Formerly, resident in urology, Massachusetts General Hospital.

our preliminary results have been so favorable, and since the successful results in some of Huggins's cases have lasted at least three years, it seems proper to present a preliminary report at this time.

As a preamble, it should be emphasized that we do not recommend this type of treatment except as an adjunct to surgery, in the treatment of those early cases of carcinoma of the prostate that permit entire removal surgically and that are without demonstrable metastases. In such cases, we carry out complete extirpation of the gland by radical perineal prostatectomy, although in addition we perform orchidectomy as a deterrent to the growth of any prostatic cancer cells that may possibly have escaped removal. Unfortunately, however, such early cases are not common, and the vast majority of cases of carcinoma of the prostate that present themselves are not only locally inoperable but frequently have metastases demonstrable by x-rays.

All but 4 of our 37 cases were definitely proved to be carcinoma of the prostate by microscopic examination of tissue, and there was convincing clinical evidence in these 4, as 2 patients had hard prostates with an x-ray picture of typical bone metastases, and the other 2 showed obstruction to urination by enlarged, hard and irregular prostates that became much smaller and softer within a few months after castration. We have recently been using the biopsy needle, as described by Silverman,¹⁰ through the perineum, with some little success in establishing the diagnosis of carcinoma of the prostate in debatable cases, and in the future there should be no case in which tissue is not obtained for pathologic examination. Eight of the 37 cases were treated simply by the administration of the potent synthetic estrogen, diethylstilbestrol, or the closely related diethylstilbestrol dipropionate—both hereinafter referred to simply as stilbestrol.

In selecting an estrogenic substance, we chose two cases were treated with castration alone, while the remaining 27 cases (73 per cent) were treated with a combination of castration and stilbestrol. the synthetic estrogen, stilbestrol,* partly because others had reported success with its use, partly because it was less expensive than the natural estrogens, and partly because in addition to being highly effective when injected, it is also much more potent when taken by mouth than an equal amount of any oral preparation of a natural estrogen, it being considered that only twice the dose must be taken orally to produce the same effect as by injection. At first, we employed diethylstilbestrol or diethylstilbestrol dipropionate in the treatment of our cases, but since we were unable

to detect any significant difference in effect between the two, we used the dipropionate almost entirely in the last three quarters of the series.

Our original plan had been to use castration alone, unless this was refused by the patient, but we then found that stilbestrol increased the castration effect markedly, giving a much more rapid and marked effect than castration alone. For instance, 2 of our early patients, two months and three months respectively after castration, had improved markedly in general condition, but had not shown much reduction in the size of their prostates. However, after ten days of intensive therapy with injections of stilbestrol their glands became markedly smaller and softer. In view of this we used a combination of castration and stilbestrol in all but the early cases. We also found that the results from stilbestrol without castration were in every way the equal of those from stilbestrol with castration. However, the effect of castration, even if slow, is permanent, whereas if stilbestrol alone is used the effect lasts only during its administration and symptoms soon return if it is discontinued, and therefore patients have to be carried on a small oral maintenance dose indefinitely; this we have done in some cases for many months without any obvious deleterious effect.

In evaluating the worth of any new form of therapy, it must first be shown that the therapy is beneficial, and secondly that the beneficial effects outweigh any unfavorable ones. In dealing with cases of incurable carcinoma of the prostate the results that are desirable to achieve are relief of pain, improvement in the patient's general condition and regression of the growth of the gland, with improvement in voiding ability. In almost all our cases the results along each of these lines were quite satisfactory.

Perhaps the most immediate and striking result of treatment was the rapid relief from the severe pain due to metastases. In 12 (32 per cent) of our cases, all but 1 of which had metastases to the bones of the pelvis or spine demonstrable by x-ray, pain was a prominent feature. In 11 of these the pain was quickly and almost completely relieved—in 1 case by castration alone, in 4 cases by stilbestrol alone, and in 6 by castration and stilbestrol. Sometimes the rapidity of the relief was astonishing. One patient got complete relief within twenty-four hours after castration, another experienced the same thing within three days, while the severe pains of a third vanished in five days after the injection of a total of 10 mg. of stilbestrol. A man of eighty-four, who had been bedridden on account of agonizing pain in the spine and legs, got up for the first time in four months after 100 mg. of stilbestrol had been injected in ten days. A patient

*The diethylstilbestrol and diethylstilbestrol dipropionate were kindly supplied by the Department of Medical Research, Winthrop Chemical Company, New York City.

with metastases to the spine and pelvis had a pathologic fracture of the first lumbar vertebra that kept him miserable and in constant pain. After castration followed by 135 mg of stilbestrol, his pain, which was rather slow to subside, had gone completely in seventeen days. When he was seen one month later he had discarded his brace which he had been

The effect of the treatment on the prostate itself was quite marked, and the gland was observed to become both smaller and softer in all but 6 cases. In 4 of the latter, the follow up time was too short to shrinkage and softening to have taken place, although their later occurrence is possible and even quite probable. However in the other 2 cases

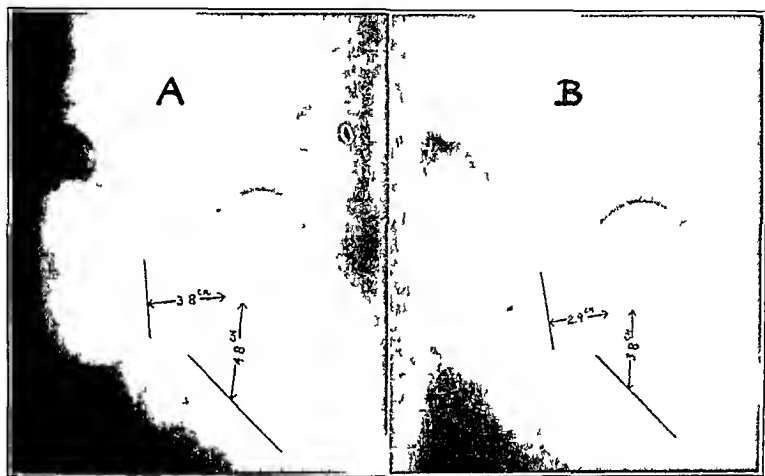


FIGURE 1 Cystoproctograms Showing Reduction in Size of the Prostate after Treatment

- A—Before treatment the prostate was somewhat enlarged and had biopsy showed adenocarcinoma. Voiding was difficult and the residual urine was 180 cc. Metastases were present in the spine and pelvic bones. The acid phosphatase was 448 Bodansky units per 100 cc.
- B—Nineteen days after orchiectomy and after the injection of 115 mg of diethylstilbestrol the prostate felt much softer as well as smaller. Voiding was normal with a negligible residual urine. The acid phosphatase was 42 Gutman units and the alkaline phosphatase 333 Bodansky units per 100 cc.

wearing for the pathologic fracture, had a good appetite and had gained weight, and said he was a different man. Seven months later the improvement had been maintained. All but 3 of these 11 patients have been seen recently and have continued to be free from pain.

After the relief of pain, the next most noticeable effect of this treatment was the almost universal improvement in appetite, weight, strength and feeling of well being, which occurred in all but 3 cases. Before therapy many patients were miserable and cachectic, and had disturbances of gastric function ranging from anorexia to nausea, often with considerable loss of weight. Within a few days they began to feel better and their appetites improved with such complete regularity that the change seemed like a physiologic response. As a result there was a noticeable gain in weight

in a reasonable trial with castration and stilbestrol. It failed to cause shrinkage and softening so that they must be considered as having definitely failed to react to the treatment. In 4 cases of the series the prostate virtually disappeared, leaving only a small soft remnant. The degree of softening, although it was marked in most cases, varied, and there were a few glands which, while definitely softer, remained fairly firm during the period of observation.

To convince those who might be skeptical of such remarkable diminutions in size, especially when determined by rectal palpation which is admittedly subject to the individual variations of examiners, the prostate was measured both before and after treatment in a number of cases by the method of Pearson and Wilson¹¹ and the reduction was demonstrated graphically by x-ray

Having discovered how markedly and rapidly stilbestrol reinforced and augmented the castration effect and reduced the size of the prostate, we car-

unable to void satisfactorily after receiving 100 mg. of stilbestrol in ten days or two weeks, it seemed a needless extravagance to prolong his hospital stay

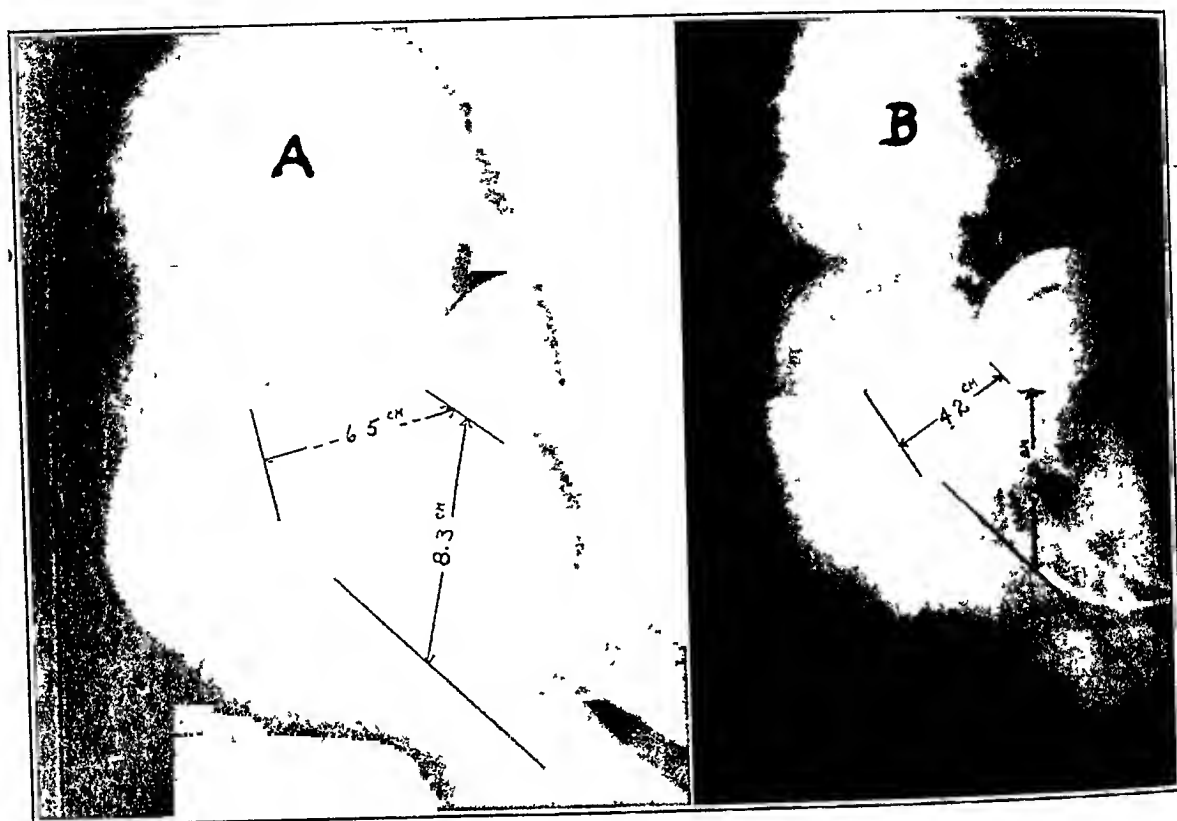


FIGURE 2. Cystopneumograms Showing Reduction in Size of the Prostate after Treatment.

A—Before treatment, the prostate was greatly enlarged and stony hard; biopsy showed adenocarcinoma. Voiding was difficult, and there was a residual urine of 500 cc. Metastases were present in the pelvic bones and spine, with a pathologic fracture of the first lumbar vertebra. The patient could not move about in bed without agony. The acid phosphatase was 39.5 Gutman units, and the alkaline phosphatase 13.5 Bodansky units per 100 cc.

B—Twenty-one days after orchidectomy and after the injection of 135 mg. of diethylstilbestrol, voiding was normal, with no residual urine. The prostate was not only much smaller but markedly softer and no longer felt like carcinoma. The pain was greatly improved, and the patient was up out of bed. The acid phosphatase was 7.5 Gutman units, and the alkaline phosphatase 32.6 Bodansky units per 100 cc.

ried out the following procedure in 13 cases of inoperable carcinoma with retention of urine. The patient was put on constant catheter drainage, and after preliminary laboratory and x-ray studies bilateral surgical castration was carried out by the intracapsular technic. Shortly after this, a series of injections of stilbestrol was started, 10 mg. being injected intramuscularly every day for five to ten days. By that time favorable effects had usually commenced, including relief of pain, shrinkage in the size of the prostate and improvement in ability to urinate. This treatment was so effective that 9 of these 13 patients who had been admitted with moderate or marked inability to urinate were enabled to void freely, did not have much residual urine and therefore never had to undergo a prostatic operation. However, if a patient was still

for further injection therapy, and he was subjected to transurethral resection.

Determinations of the acid phosphatase were made on 20 patients before and after castration. Our findings confirmed those of Huggins.^{1,2} In every case where the acid phosphatase was definitely above normal (7 cases), the level fell very rapidly following castration, and was still further reduced following intensive injection therapy with stilbestrol. Our findings also agreed in general with those of Robinson, Gutman and Gutman³ and those of Huggins in that 5 of the 7 cases with elevated acid phosphatase had roentgenologically demonstrable metastases to bone. However, the metastases did not necessarily cause an elevation, as there were cases with metastases demonstrable by x-ray in which the acid phosphatase level

was normal. Thus it would appear that elevation of the acid phosphatase, if present, strongly indicates metastases, but that a normal value for acid phosphatase does not necessarily rule them out. There seemed to be no definite correlation between the elevation of the acid phosphatase and pain. Six of the 12 cases where pain was a prominent feature had determinations of the acid phosphatase before treatment, and this was elevated in only 1. In this case, following castration and estrogenic therapy, the level came down to nearly normal within one week—ten days before the pain was fully relieved. Furthermore, the patient who had the highest acid phosphatase level of any of our series (44.8 Gutman units per 100 cc.), with widespread metastases to the pelvis and spine, had absolutely no pain. His acid phosphatase decreased to 10 Gutman units within six days after castration. The original level had no prognostic value regarding the probability of the success of the treatment, as favorable results were obtained in cases with both normal and elevated values. The level in the 1 case that was apparently not benefited at all was approximately normal, and was not reduced by the treatment.

Estimations of the alkaline phosphatase were made before and after castration in 22 cases, elevated values being found before operation in 10 of these. In 8 of the 10, bony metastases were demonstrable by x-ray, 1 had extensive Paget's disease, and in 1 case the x-ray films were equivocal. Our experience agreed with that of Huggins in that there was usually a rise in the alkaline phosphatase shortly following castration, either with or without stilbestrol.

Measurements of the 17-ketosteroids were made before and after castration in 23 cases. As was to be expected, in most cases they decreased after orchidectomy. In several cases where they did not, the acid phosphatase had decreased and the patients were doing well clinically. Conversely, 2 patients who did poorly (1 of them died) had 17-ketosteroids that became low after castration and remained low for several months afterward, during which time their metastases were increasing and their general condition was worsening. Therefore our general impression is that the measurement of the 17-ketosteroids does not give information of great value in the management of cases of carcinoma of the prostate.

Despite the almost universal relief of the pain of metastases by this treatment, we have not yet been able to detect any roentgenologic evidence of favorable effects on bony metastases, such as inactivation or regression, as have been described by some authors. In 5 cases followed for more than six months (4 of which received castration and stil-

bestrol therapy, and 1 stilbestrol alone), x-ray films have shown the bony metastases to be apparently progressing as usual. A longer follow-up period is needed for us to come to any decision of value.

Of the 37 patients in the series, only 1 was apparently not benefited in any way by this treatment. Despite the fact that he had had castration followed by large amounts of stilbestrol, both by injection and orally, he experienced no relief from his moderate amount of back pain, very little reduction in the size or induration of the prostate and absolutely no improvement in his general condition, which deteriorated progressively. This case was peculiar in that, despite very extensive metastases to the spine, liver and other viscera found at autopsy, the acid phosphatase before any treatment was given was only 4.6 Gutman units per 100 cc.—essentially normal. Furthermore the level was not reduced by castration and stilbestrol therapy. Two days before death, when the patient had been without stilbestrol for twelve days, the acid phosphatase rose to 14.6 Gutman units. That this was a case of carcinoma of the prostate there is absolutely no doubt, as the clinical findings were those of that disease, and the microscopic sections were thus diagnosed by several pathologists.

In addition to the case just described 2 other patients died. In 1 case, with extensive bony metastases, the progress of the disease was halted for six months by castration and stilbestrol. After that time, however, despite the administration of stilbestrol, and although the prostate did not grow, the general condition became worse, and the patient died about a year after castration in a state of profound anemia and weakness. The third patient to die was killed in an automobile accident two weeks following castration, so that sufficient time had not elapsed to evaluate the effect of treatment. Thus out of the 37 patients seen in one year, only 3 died, 2 of their disease and the third from an accident. Of the remaining 34, all but 5 have been seen fairly recently, and all are getting along well; they are in good general condition and have no pain, and none of them look as though they were going to die for a long time.

When it comes to a consideration of the unfavorable effects of castration, it must be said that libido and power of erection never reappeared after orchidectomy in the vast majority of cases. However, to blame this entirely on castration is perhaps not fair, since many of these sick, elderly men had not been sexually active for a long time before castration. No other harmful effects of castration were noted on either mind or body.

To lessen the likelihood of mental distress arising from the feeling of patients that by castration they had been deprived of their manhood, bilat-

eral orchidectomy was in most cases performed by a special technic, which we have called "intracapsular orchidectomy." We began using this technic more than a year ago and have now applied it to nearly 40 cases, having done all our orchidectomies in this manner for the last nine months. After the testis has been exposed surgically, a generous incision is made in the tunica albuginea, and the soft, stringy, tan-colored testicular substance is easily separated with gauze dissection from the inside of the tunica down to the mediastinum. Here the blood vessels, which form a sort of pedicle, are clamped and ligated en masse and the testicular substance is cut away. The incision in the tunica is then sutured. In this way the functioning substance of the testis is removed, but there remain the spermatic cord, the epididymis and the oval mass formed by the sutured tunica albuginea, and the patient is not left with an empty and shrunken scrotum as is the case following the usual type of bilateral orchidectomy. Physical examination after this procedure usually gives the impression that the testes are present although very small. On casual examination the patient finds what appear to be small but normal testes. As a result, although he knows that the essential part of the testes has been removed, he does not feel that he has been completely castrated, as he is sure to feel with an absolutely empty scrotum. This may seem to be a minor point, but it may be of considerable psychologic importance in the avoidance of depression in morbidly introspective patients.

As to the unfavorable effects of stilbestrol therapy, there were several, but none of them were very serious. Again, as after castration, the vast majority of those taking the drug lost their libido and power of erection. Also, all those taking stilbestrol, especially those given small oral maintenance doses over a period of weeks or months, developed tenderness, hypertrophy and sometimes pigmentation of the nipples, and frequently some hypertrophy of the whole breast. This was usually not too bothersome; it could be lessened by cutting down the dose, and soon disappeared when the drug was discontinued. Another almost universal effect was that the testes, if present, became definitely smaller. A number of patients while receiving intensive stilbestrol therapy developed edema of the ankles and lower legs, which disappeared when the dose was decreased. A very few also complained of cramps in the legs during intensive injection therapy. Surprisingly few complained of anorexia or nausea, although this occurred in scattered cases, necessitating the temporary discontinuance of the drug or a reduction of the dose. No other unfavorable effects were noted. Therefore, in view of our experience we favor

supplementing orchidectomy with stilbestrol therapy for some weeks or even months thereafter.

As regards the advisability of intensive or prolonged administration of stilbestrol, there have been reports in the literature, based largely on experimentation with small animals, suggesting that such administration might be dangerous. Since it has been shown that stilbestrol is normally detoxified in the liver, attention has been focused on this organ as the most likely to show toxic changes, and huge amounts of stilbestrol—sometimes several thousand times the physiologic estrinizing dose—have been administered to experimental animals in efforts to answer this question. Although not unanimous, the trend of recent opinion is that even very large doses of stilbestrol are relatively harmless to the liver. The harmful effects that have been reported in laboratory animals following administration of tremendous doses include anemia and neutropenia, changes in the pituitary and adrenal glands, and the occurrence of pituitary, mammary or testicular tumors in cancer-strain rats and mice. These changes, however, have been mostly produced by the administration of huge amounts of stilbestrol—hundreds of times the physiologic dose given to man—and recent papers by Grauer and Nugent,¹² Morrell and Hart¹³ and Russell and his co-workers¹⁴ tend to substantiate the growing clinical opinion that, in the doses commonly given to man, stilbestrol does not have harmful effects. Certainly no dangerous or harmful effects were noted in any of our cases. One of our patients who died with widespread metastases to bone and viscera showed absolutely no evidence of toxic liver damage, although in addition to castration he had received 100 mg. of stilbestrol intramuscularly and 200 mg. orally during the six weeks preceding death.

At the present time the following procedure is used in cases of inoperable carcinoma of the prostate. If the patient has much retention of urine, he is put on constant catheter drainage. After preliminary laboratory and x-ray studies, bilateral orchidectomy is performed by the intracapsular technic. In cases with much retention of urine, although we know that by using intensive stilbestrol therapy in addition to castration we can probably in ten days or so shrink the prostate enough so that the patient can void and empty the bladder much better, we now consider this an unnecessary and extravagant prolongation of the hospital stay, and perform transurethral resection at the time of the orchidectomy or shortly thereafter. While in the hospital, the patient receives an intramuscular injection of 10 mg. of stilbestrol every day for five to ten days, if tolerated, to give the endocrine process acting on the pros-

tate an additional impetus beyond that conferred by castration alone. When the patient goes home he is put on a dosage of 1 mg. of oral stilbestrol two or three times a day for two months.

In view of the experiences and results described, we believe that this type of therapy gives a great deal of promise in the treatment of inoperable carcinoma of the prostate.

SUMMARY

Reducing the action of androgens in the body, either by surgical castration or by biochemical neutralization through the administration of the synthetic estrogen, stilbestrol, or a combination of the two, was used in treating 37 cases of inoperable carcinoma of the prostate during the period July, 1941–July, 1942.

Two cases were treated with castration alone and 8 cases by stilbestrol alone. The effect of castration was accelerated by the addition of stilbestrol therapy, and this combination was used in 27 cases (73 per cent). The results of stilbestrol therapy alone were in every way the equal of those of castration and stilbestrol, but the effect of stilbestrol alone lasted only during its administration.

The general results were very satisfactory, and only 1 patient seemed to receive no benefit at all from the treatment. Three patients died during the year.

The beneficial effects included rapid, effective and lasting relief from the pain of metastases, improvement in appetite, weight and strength and a feeling of well-being, and reduction and softening of the prostate.

In 9 of 13 cases with inability to urinate and retention, treated with orchidectomy and stilbestrol, the size of the obstructing prostate was so reduced that the ability to void returned.

Determinations of the acid phosphatase showed that when the level was above normal preoperatively it fell rapidly after castration, and was still further reduced by stilbestrol therapy.

The alkaline phosphatase usually rose shortly following castration, with or without stilbestrol.

The 17-ketosteroids were lowered in most cases after orchidectomy. The level seemed to have no relation to the course or progress of the disease.

In 5 patients with bony metastases demonstrable by x-ray who were followed for more than six months, the metastases were apparently progressing as usual.

After castration, libido and power of erection disappeared in most cases, but there were no other harmful effects.

No dangerous or harmful effects were noted from stilbestrol therapy, either from intensive injection therapy or from long-continued oral therapy. There were, however, minor unpleasant effects. All these soon disappeared if the drug was discontinued or the dose decreased.

A new technic of cosmetic intracapsular orchidectomy is described.

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THE CARE OF PATIENTS REQUIRING THYROIDECTOMY

OLIVER COPE, M.D.,* AND CLAUDE E. WELCH, M.D.†

BOSTON

THE Massachusetts General Hospital, under the supervision of the Thyroid Clinic, trains interns and residents in the care of patients with disease of the thyroid gland. Written instructions for the guidance of the House Staff maintains continuity of the standard of care and teaching. The directions dealing with patients to be treated by operation are given below, in the hope that they may prove useful to other hospitals and physicians.

To keep the operative mortality of patients with goiter, and especially with hyperthyroidism, at the lowest possible level, the following recommendations should be kept in mind.

CLASSIFICATION

On both the medical and surgical services an estimate of the operative risk of each patient should be made. Whether hyperthyroidism is present must first be settled — masked hyperthyroidism in older people is easily overlooked. It also should be appreciated that an elderly patient with an obstructing goiter without thyrotoxicosis may present just as great an operative risk as a younger patient with thyrotoxicosis.

Patients are grouped in three classes according to operative risk:

Class A — Good Risks: Patients with uncomplicated nontoxic goiter, and young patients with toxic goiter of mild intensity.

Class B — Medium Risks: Patients with uncomplicated, moderately severe toxic goiter, with obstructing or mediastinal goiter and with cancer of the thyroid gland.

Class C — Poor Risks: Patients with thyrotoxicosis who present any of the following criteria of inability to stand operation well; extreme intoxication indicated by high basal metabolic rate, severe symptoms or crisis status; a rising basal metabolic rate; poor or absent iodine response; failure of the pulse rate to drop on bed rest and iodination (that is, lack of cardiac reserve); the presence of cardiac complications, such as insufficiency, fibrillation, hypertension and a valvular lesion, or a history of paroxysmal fibrillation or tachycardia; a poor nutritional state, including inability to gain weight in the

hospital; an active infection; a psychotic state; and old age.

The last class also includes patients in the older age groups with severe obstructive symptoms without thyrotoxicosis.

PREOPERATIVE CARE

The following points apply in some degree to all patients who are to have a thyroidectomy. Their fulfillment is mandatory in Class C patients; judgment must be used in their application to Class A or B patients.

- (1) Patients must be fully iodinated and have been on bed rest long enough to build up a maximum cardiac reserve.
- (2) Patients must be free from active infection, throat or other. Sulfonamide therapy should be instituted only after due consideration of the concept that toxic reactions to sulfonamide drugs are peculiarly undesirable in thyrotoxic patients who are already suffering from a nutritional handicap and an impending hepatic insufficiency. Sulfonamides are indicated in severe, acute infections that threaten to produce a thyroid storm, and in certain persistent subacute infections. A long interval of hospitalization should intervene between drug therapy and operation, particularly if a toxic reaction has occurred. Rarely should sulfonamides be used as an immediate preoperative preparation. Local use of sulfonamide powder in the wound at operation may be warranted, but in general if infection exists in the neck, thyroidectomy must be postponed.
- (3) Preoperative preparation should be long enough to ensure a good nutritional reserve, as well as to dissipate any deficiency. Measures must be taken to build up stores of vitamins, protein and liver glycogen. An increase in all foodstuffs, proportionate to the elevation of the metabolic rate, is required.
- (4) Nembutal, luminal and Amytal are advised for sleeplessness. Paraldehyde may be used, but occasional excitement ensues. Bromides, as well as luminal in small doses, are useful for restlessness. Codeine is permissible for cough, and with aspirin for pain. Morphine, Pantopon and Dilaudid are reserved for crisis and preanesthetic preparation. Chloral hydrate is

*Assistant professor of surgery, Harvard Medical School; associate visiting surgeon, Massachusetts General Hospital.

†Assistant in surgery, Harvard Medical School; assistant surgeon, Massachusetts General Hospital.

contraindicated in the presence of cardiac difficulty and is therefore rarely useful in thyrotoxicosis. Atropine should be used with caution in view of its vagal inhibitory effect.

- (5) Throat consultation is required to exclude contraindications to intratracheal anesthesia (ulcers or inflammation), as well as to determine any pre-existing cord palsy. If the resident and anesthetist are satisfied by inspection that the larynx is normal, consultation by a laryngologist may be omitted in Classes A and B.
- (6) Chest roentgenograms to determine the presence of intrathoracic goiter and anteroposterior and lateral plates of the neck to check tracheal displacement and narrowing are necessary only if configuration of the palpable goiter is in doubt. Fluoroscopy and a 7 foot plate of heart are required if the cardiac findings are disproportionate to the metabolic rate.
- (7) An electrocardiogram should be taken if the heart findings are not accounted for by the thyrotoxicosis.
- (8) Digitalis and a longer rest period, a minimum of three weeks, are required in patients with congestive failure. Digitalis should also be given to all patients in whom auricular fibrillation persists after iodination and bed rest; it should be discontinued after operation, when the hyperthyroidism has been relieved, to remove its stabilizing effect on the fibrillation. Digitalis is advisable in patients in the older age groups with no failure and with regular rhythm whose cardiac capacity is small or no greater than the load. Such digitalization helps to counterbalance the additional burden of operation.
- (9) Quinidine, pre- and postoperatively, should be considered in cases with a history of paroxysmal fibrillation or tachycardia; it should be given to all cases in Class C except those with active auricular fibrillation. It should be started twenty-four hours before operation and continued until the load on the heart is sufficiently relieved to make fibrillation unlikely, usually twenty-four to thirty-six hours after operation.
- (10) The anesthetist should be consulted regarding the choice of anesthesia and any basal medication to be given on the ward.
- (11) These patients must be operated on early in the morning; the operation must not be postponed except for the patient's own good.

Reassurance of patients with thyrotoxicosis before operation regarding the entire operative pro-

cedure is most important. They should be informed concerning what to expect of the anesthetic, postoperative discomfort, intravenous injections and the oxygen tent. The use of the term "air conditioned tent" producing cool, moist air for sore throat is suggested. If such reassurance is inadequate a preoperative trial of the tent is indicated.

Crisis

The course of hyperthyroidism is subject to exacerbations and remissions. If an exacerbation comes on acutely with severe symptoms, the episode is called a thyroid "crisis" or "storm." To a more rapid pulse rate and pounding heart there may be added a high fever and a physical and emotional instability difficult to control. It is as if the smoldering fire of the thyrotoxicosis had suddenly been fanned to flame. If the storm is progressive, death may occur suddenly. The fever increases the metabolic rate, nutritional deficiency develops rapidly, and it is believed by some that hepatic insufficiency is the cause of death.

A crisis may occur at any time during the disease. It may be induced by an acute infection or severe emotional strain before operation. The commonest causes are operation itself and the postoperative complications. Until the thyrotoxicosis is relieved, the threat of a storm must be kept in mind. No matter when it occurs, the treatment is symptomatic, except for the administration of iodine. Reassurance and sedation for the instability, ice packs for the fever, an oxygen tent and every effort to maintain nutrition are indicated. The use of iodine should be instituted immediately if it has not been given; it should otherwise be continued. Nothing is gained by increasing the dosage provided that the previous doses have been sufficient to saturate the gland.

OPERATION

Anesthesia

Adequate oxygenation in thyrotoxicosis is the paramount consideration, and a free airway must be maintained no matter which agent is used. Hyperextension of the neck, necessary for good exposure of the thyroid gland, tends to produce laryngeal obstruction. Tracheal constriction is a hazard of the induction of either local or general anesthesia. Tracheal obstruction may occur, and the surgeon should be prepared to open the neck rapidly.

The base line of the patient's reaction to removal to the operating room should be obtained before any anesthetic agent is started. The pulse and blood pressure should be followed at five minute intervals while the patient is being transferred to

the operating table. When general anesthesia (ether) is used, the induction should not be hurried, and it is wise to wait until the patient is stabilized under the anesthesia before starting the operation. Undue emotional reaction caused by being taken to the operating room should disappear under the anesthetic agent. If it does not, the operation should be postponed. The operation should not be begun until one is sure of the patient's condition.

Agents of choice. Local procaine is useful for patients in Class A with a bilateral operation, and in Class C patients in whom preoperatively it is possible to decide that a hemithyroidectomy is advisable. A satisfactory bilateral operation under local anesthesia requires considerable basal anesthesia of barbiturates and opiates; adequate oxygen intake is sometimes hampered during and after operation by such heavy medication and is therefore contraindicated in Class C risks. Adrenalin should not be added to the procaine solution; the thyroid hormone sensitizes the heart to adrenalin, and the likelihood of fibrillation is increased.

A preliminary trial of the medication to be used in the basal anesthesia is sometimes advisable. The best way, however, to judge the dosage of barbiturates and opiates required is to observe the reactions of the patient during the period of administration. The initial medications should be given one and a half to two hours prior to the time of operation, and subsequent doses as needed.

Oxygen, nitrous oxide and ether, given intratracheally, is preferable, and is indicated in Class C. The one contraindication of an intratracheal tube is that it may increase the incidence of laryngeal edema and obstruction. Three measures should be taken to decrease laryngeal edema when an intratracheal tube is used. First, the tube must be inserted under direct vision without trauma; secondly, particular care on the part of the surgeon must be taken to avoid trauma to the trachea and larynx and to avoid distorting the trachea while the tube is in place. Thirdly, patients with preoperative laryngitis requiring an intratracheal tube should have only a hemithyroidectomy, to maintain adequate venous and lymphatic return to at least one side of the larynx.

Permissible agents. Nitrous oxide (70 per cent) and oxygen (30 per cent) may be used as an adjunct to local anesthesia when the airway is unobstructed. Such anesthesia will not permit use of an intratracheal tube.

Agents absolutely contraindicated in thyrotoxicosis. Cyclopropane may induce ventricular fibrillation in patients with thyrotoxicosis. Avertin produces inadequate oxygenation through direct effect on the circulatory system and the respiratory cen-

ter; it also causes liver damage, an effect particularly undesirable in patients with the impending hepatic insufficiency of thyrotoxicosis. The toxic effects of Avertin are similar to those of chloroform and ethyl chloride, and include, besides those above mentioned, damage to the renal tubules and possibly ventricular fibrillation.

Extent of Excision

Thyrotoxicosis is caused by two types of disease process. The rare one is hyperfunctioning adenoma, a form of neoplasia; excision of the adenoma alone is indicated since the rest of the gland is uninvolved and is indeed atrophied from disuse. The common type is the diffuse hyperplasia or its involutional result; the amount of tissue to be excised to relieve the thyrotoxicosis and the amount to be left to maintain normal thyroid hormone production vary with the existing degree of hyperplasia, the involution and the ability of the patient to produce regeneration of the thyroid remnant. In general the remnant should be larger when the tissue is well involuted and the thyrotoxicosis mild. It is wise, when in doubt, to err on the side of too radical an excision.

Stage or divided operations are sometimes indicated. With the means of preparation for operation now available, pole ligations are rarely resorted to. Division of the operation into two parts, subtotally resecting one lateral lobe at a time, is indicated in Class C patients with persistent cardiac insufficiency. If the reaction to the anesthetic and operation is greater than anticipated, stage procedures should be used in less sick patients. A continuous rise in the pulse rate and blood pressure during the course of the operation should serve as a warning. A pulse rate of 160 and a systolic pressure of 40 mm. above the preoperative level should be considered maximal heights before terminating the operation.

The surgeon must use his own judgment during the operation concerning how far to proceed. The object should always be to do as much of the subtotal excision as the patient's condition warrants. At least one week should intervene between operations, but in general the second operation should not be performed until the patient has received the maximum benefit from the first.

POSTOPERATIVE CARE

Supervision

Most important to the successful outcome of a thyroid operation is careful watching during the first two days after operation. It is the time of crisis. The excessive thyroid function has not as yet been decreased and the burden of operation and its attendant excitement have been added to

the already taxed organism. The majority of severe cardiac complications, such as fibrillation, flutter or tachycardia with break in compensation, occur in the eight hours immediately after the patient has left the operating room, not during the operation. Hemorrhage and laryngeal edema may not occur until twenty four hours have passed.

The pulse and blood pressure should be carefully followed. A continued rise suggests anoxemia from laryngeal obstruction.

Stridor must be listened for. If it persists when the patient is awake, it warns of concealed hemorrhage with pressure and beginning laryngeal edema, or bilateral-cord palsy. Both may prove to be rapidly fatal lesions, and immediate return of the patient to the operating room and prompt exploration of the wound and visualization of the larynx are indicated. Either cause of laryngeal obstruction usually demands tracheotomy even though the hemorrhage is relieved.

An oxygen tent immediately is indicated for all Class C risks, and should be continued for at least twenty four hours or longer if reaction to the operation continues. It is advised for Class B patients if there has been an undue rise in pulse or blood pressure during operation, but may be abandoned sooner if the untoward signs subside promptly. Increasing the oxygen tension of the inspired air relieves in part the burden of the circulatory system, already overloaded by the demands of thyroid hormone and operation. Should postoperative infection occur, either in the lung or in the wound, the tent should be reinstituted, since infection causes an additional rise in metabolic rate.

Glucose and salt solution should be given intravenously, slowly, to all Class B and C patients in the first six hours. Glucose must be continued during the first forty-eight hours if drinking by mouth is inadequate on account of pain or nausea. High carbohydrate, protein and vitamin intake should be resumed as quickly as the patient tolerates it.

Iodinization should be resumed as soon as the patient can drink comfortably. Since previous iodination has already saturated the gland, nothing is gained by giving iodine intravenously or by mouth immediately after operation. It is resumed within a few days to replace that which is slowly excreted. If the metabolic rate is below normal within two weeks after operation, iodine may be omitted, otherwise, it should be continued until it is certain that a normal or subnormal metabolic rate has been established.

Special nursing for Class C patients is usually desirable.

Aspirin water and benzoin inhalations are given for throat symptoms. Icecaps may be tried.

Transfusion is ordinarily indicated only when postoperative hemorrhage has occurred. It is rarely a part of the preoperative preparation, and since hemorrhage at operation should not occur with the modern careful technic of thyroidectomy, it is not part of the routine care of patients with thyroid disease.

Postoperative parathyroprival tetany is to be differentiated from hyperventilation tetany by the blood calcium level and the effect of rebreathing. When parathyroid glands are sought and spared, not blindly avoided, at thyroidectomy, postoperative tetany is rare. When at least one parathyroid gland has been seen and not injured, if tetany occurs, it is probably due to hyperventilation. Reassurance is usually adequate therapy. For low-calcium tetany, calcium gluconate or chloride is indicated, by vein or mouth, such tetany must be treated promptly and vigorously to prevent laryngeal spasm.

The patient should be discharged to the Thyroid Clinic for follow up.

* * *

The following outline, based on the preceding instructions, has been prepared for the guidance of interns and residents in the care of patients with diseases of the thyroid gland requiring operation. It is recommended that frequent reference for details and reasoning be made to the more complete instructions, a copy of which is on each ward.

CARE OF PATIENTS REQUIRING THYROIDECTOMY

The operative risk of each patient should be determined. Class A (good), Class B (medium), and Class C (poor). Symbols: + = obligatory, * = advisable.

PREOPERATIVE ROUTINE

Class			
A	B	C	
+	+	+	Full iodimization in thyrotoxicosis
		• +	Prolonged bed rest.
+	+	+	No operation in presence of infection or recent sulfonamides
+	+	+	Nutrition: high protein, carbohydrate and vitamin intake
		• +	Consultation concerning throat condition
		• • +	X ray films of thyroid gland and chest.
		+	Electrocardiogram
		• +	Quinidine, except in presence of persistent fibrillation
		+	Digitalis in persistent fibrillation failure or impending failure
+	+	+	Reassurance
		+	Medication (see detailed instructions)
		+	Consultation concerning anesthesia
		• •	Trial of medications, if local anesthesia is to be used

* * * Preoperative transfer to surgical ward for two to three days, the patient's condition being weighed by consultation between the services.

+ + + When hyperthyroidism is diagnosed on medical service, surgical resident to be notified.

+ + + No operation in presence of psychotic state.

OPERATIVE ROUTINE

- (1) Enema only if needed, and then always the night before.
- (2) Sedation the night before.
- (3) Preparation to be done the morning of operation; to be completed not later than fifteen minutes after the initial medication.
- (4) Preoperative medication. Nitrous oxide, oxygen and ether: 1/6 gr. morphine and 1/150 gr. atropine; Nembutal permissible. Local: Nembutal and morphine, starting one and a half to two hours before operation, in doses depending on the somnolence desired.
- (5) Operation to be postponed or discontinued if response to preoperative medication unsatisfactory, if anesthetic agent not tolerated (cyanosis not relieved by intratracheal tube or pulse or blood pressure

over 160), if respiratory difficulty (under local anesthesia) or if change in voice (under local anesthesia).

POSTOPERATIVE ROUTINE

Class

A B C

- | | | | |
|---|---|---|--|
| | * | + | Oxygen tent. |
| + | + | + | Intravenous glucose and salt. |
| + | + | + | Pulse and blood pressures to be taken hourly for at least twelve hours and until condition is stabilized; sudden changes to be reported. |
| + | + | + | If stridor, report immediately and open wound. |
| + | + | + | If difficulty in swallowing, observe closely for hemorrhage. |
| + | + | + | Tracheotomy set on floor. |
| + | + | + | Special nurses; otherwise, patient to be on open ward. |
| + | + | + | Carbohydrates, proteins, vitamins and iodine to be resumed as patient can swallow. |
| | | | Aspirin gargle, benzoin inhalations and ice cap, as desired. |

MEDICAL PROGRESS

DIGITALIS, EDEMA AND DIURETICS*

A. STONE FREEDBERG, M.D.,† AND HERRMAN L. BLUMGART, M.D.‡

BOSTON

DIGITALIS

THE proper use of digitalis requires a clear understanding of the strength of the preparation used. It is unfortunate, therefore, that considerable confusion and misunderstanding prevail at the present time. The meaning of the descriptive terms by which the strength of the various marketed preparations is described on the label and the potency of these preparations when administered to patients have been discussed by various authors¹⁻⁵ in recent years, but it would seem worth while at this time to review the present status of the situation.

The eleventh revision of the *United States Pharmacopoeia* now in use§ went into effect in 1936 and attempted to make the potency of the digitalis preparations employed in the United States

comparable to that used in other countries; the strength of digitalis was defined in terms of the "international standard reference powder" of the League of Nations. The international reference powder was assayed by the cat method; the official method of assay of *U.S.P. XI* is the one-hour frog method. It was generally believed that the change made in *U.S.P. XI* would lead to an increase in potency to 125 to 130 per cent of the digitalis official in the preceding pharmacopoeia. Biologic assays as well as clinical experience have shown, however, that the increase in potency was greater than anticipated and amounted to as much as or more than 50 per cent. This increased potency of digitalis of *U.S.P. XI* has not been fully appreciated by many physicians and has led to frequent toxic reactions. The situation was, and still is, further complicated by the fact that, although certain manufacturers have continued to market digitalis of the potency of *U.S.P. X*, others have increased the strength of their preparations to approximately 150 per cent in an attempt to conform to *U.S.P. XI*. It is important, therefore, that the physician note whether the potency of the digitalis that he prescribes is described in terms of *U.S.P. X* or *U.S.P. XI*.

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*From the Medical Service, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School.

†Assistant in medicine, Harvard Medical School; associate in medical research and junior visiting physician, Beth Israel Hospital.

‡Associate professor in medicine, Harvard Medical School; director of medical research and visiting physician, Beth Israel Hospital.

§Since this paper was submitted for publication, *U.S.P. XII* has become official. The potency of digitalis *U.S.P. XII* is stated elsewhere in this paper.

Apparently to avoid these difficulties, some manufacturers simply state the strength of the preparation in terms of cat units without reference to the pharmacopoeia. Although the cat method of assay has advantages and more nearly parallels the therapeutic potency in man than assays by the one-hour frog method, many variables are inherent in the technic. Among these are the depth and type of anesthesia, the speed of injection and the inherent differences of various cats, which can be only partially negated by using a series of animals. One must recognize, moreover, that preparations of the same potency in regard to their ability to kill a cat may vary markedly in their therapeutic activity in man. This is partly because the cat method of assay involves intravenous injection and consequently fails to distinguish between absorbable and nonabsorbable material. Thus, although it may require 15 to 25 cat units of digitalis leaf or tincture to digitalize a subject by mouth, 3 cat units of digitoxin—*digitaline cristallisee* (*Nat. velle*)—will accomplish the same result.⁶ In this connection, Gold et al.⁷ have recently described a method of bioassay of digitalis preparations in man which, if adopted, would ensure greater uniformity in the clinical potency of the preparations available to physicians.

The degree to which powdered leaf or tincture of digitalis deteriorates is of practical moment and has been ably studied by Gold and his associates.⁸ It has been shown repeatedly that when the tincture of digitalis is stored for months, it loses potency according to the frog method of assay. This loss may amount, within three or four months, to as much as 50 per cent. As these authors remark, physicians appear to have been misled by the method by which the loss of potency was revealed, for, according to the cat test, the tincture retains its previous strength. Tests made with a very old tincture that had "deteriorated" by the frog method showed full strength in human beings.

In the forthcoming twelfth revision of the *United States Pharmacopoeia*, a new reference powder, standardized by the cat method of assay, will be employed. The potency of digitalis will be approximately 125 per cent greater than preparations in use prior to 1936. In general, therefore, if 15 gm of powdered digitalis leaf of *U.S.P. X* is considered to be the approximate amount necessary to digitalize a 150 pound patient, only 1.0 gm of the *U.S.P. XI* preparation is necessary, whereas 125 gm will be required according to the forthcoming *U.S.P. XII*. In clinical practice, 1.0 gr. of powdered digitalis *U.S.P. XI* three times a day for three to eight days, followed by 1.0 gr., five to eight doses a week according to individual requirements, will usually accomplish effective digitalization. It

should be recalled that satisfactory clinical digitalization in any given case does not imply reaching a point, but rather a range, which may be from 40 to 75 per cent of the toxic dose.⁹

The changes to be made in *U.S.P. XII* will remove much confusion and lead to a more uniformly potent preparation. It should be remembered, however, that the variations in dosage requirements by different patients are also considerable, so that proper clinical practice will depend, as it has since the time of Withering, on the ability of the clinician to know when the therapeutic effect has been achieved and to discontinue medication when the patient experiences anorexia.

Newer Digitalis Preparations

The difficulties with standardization and the unabsorbability of certain fractions of whole leaf digitalis from the gastrointestinal tract in man already mentioned point to the need for pure crystalline chemical substances having the properties of digitalis and suitable for oral administration. Chemically pure crystalline substances can be prescribed in terms of weight of the drug, thus obviating the necessity for biologic assay. Stoll¹⁰ in 1937 described the methods of isolation and crystallization of three glycosides from *Digitalis lanata*. These are known collectively as Digiland and separately as lanatosides A, B and C. Many reports¹¹ in Europe and several in this country^{12, 13} show that Digiland, which is a mixture of lanatosides A, B and C in constant proportions, in doses of 0.2 mg., is equivalent to and interchangeable with 0.065 gm or 1.0 gr of whole leaf digitalis *U.S.P. XI*.

Reports are also available^{14, 15} dealing with one of these lanatosides, namely, lanatoside C. In man, each milligram of this drug is equivalent to 0.17 gm or 2.6 gr of whole-leaf digitalis.¹⁶ Fahr and LaDue¹⁷ used lanatoside C in 256 patients with congestive failure and noted that the drug produced rapid and effective clinical responses, whether auricular fibrillation was present or absent. Toxic reactions were rare, and a few patients who were unable to tolerate digitalis took the drug with a good therapeutic result. The oral dose necessary to accomplish therapeutic digitalization¹⁹ averaged 60 to 75 mg. (12 to 15 tablets) over a period of forty eight to seventy-two hours, and the maintenance dose was 0.5 to 2.5 mg. (1 to 5 tablets), average 1.5 mg. (3 tablets). The full digitalizing dose of lanatoside C by intravenous injection is about 15 mg. given within two or three hours. The much larger oral dose necessary to achieve digitalization indicates that the absorption of this drug from the gastrointestinal tract in man is quite imperfect. Aside from the uniformity of the preparation, Digiland and lanatoside C pos-

ness no convincing superiority over powdered digitalis or tincture digitalis *U.S.P.* for gradual digitalization of the majority of patients. The above advantage of uniformity, moreover, is negated if the physician confines himself to the use of a preparation of digitalis with whose pharmacologic properties he is familiar.

Digitoxin has been used in Europe for many years, but has not been used extensively in this country. Gold and his associates^{9, 20} recently published the results of a study of the use of this drug in 213 unselected patients with varying degrees of congestive heart failure. It was shown by them that the drug is practically completely and rapidly absorbed from the gastrointestinal tract, the average oral and intravenous dose for full digitalization in man equaling 3.0 cat units or 1.25 mg. Digitalization by the oral method is complete in from six to ten hours. The classic studies of Hatcher and his collaborators, Eggleston and Weiss,^{21, 22} have amply demonstrated that digitalis emesis as commonly encountered after repeated small doses is not the result of local irritative effects on the stomach, but is due to afferent impulses from the heart or a direct action on the central nervous system. Gold²⁰ has shown, however, that when large doses are given, the local emetic action on the gastrointestinal tract may assume importance. This effect may be largely obviated by using digitoxin. Only about 2 per cent of the patients given a full single digitalizing dose of digitoxin become nauseous or vomit, whereas approximately 20 per cent of patients given a full digitalizing dose of whole-leaf digitalis present toxic manifestations. It is apparent, therefore, that digitoxin represents an excellent drug for rapid oral digitalization. The cost is considerably higher than that for an equivalent amount of whole-leaf digitalis.

Quabain, a pure glycoside, although long in use, only now is to be included in the twelfth revision of the *United States Pharmacopeia*. Poorly absorbed from the gastrointestinal tract, it is suitable only for intravenous or intramuscular injection. An intravenous injection of 0.25 mg. repeated once or twice at intervals of two hours may produce dramatic relief of the symptoms of heart failure, and in patients with auricular fibrillation may reduce the heart rate from a level of 150 to 70. The drug is therefore useful in the occasional patient who has not been treated with digitalis and in whom rapid digitalization parenterally may be necessary. The view that strophanthin given intravenously produces effects not obtainable by digitalis has won widespread acceptance in Europe and has recently been propounded in this country. No convincing evidence exists to support such a view, provided suitable measures are invoked to

assure adequate doses of digitalis reaching the circulation.⁵

The purified mixtures of digitalis glycosides, such as digifoline, are widely used and fill a definite need when parenteral administration is indicated. It must be remembered that the digitalizing dose of digifoline, given intravenously or intramuscularly, is far less than the oral dose; thus it may require only 3 to 6 cat units of the drug intravenously to digitalize a patient. Oral administration of digitalis meets the requirements of the vast majority of cases, and the indiscriminate use of digitalis preparations parenterally is to be discouraged.

In all digitalis preparations so far studied, including lanatoside C and digitoxin, no significant difference is apparent in the margin between toxic and therapeutic doses.

In this country, chemists have succeeded in combining one molecule of a genin obtained from a squill's glycoside with two molecules of theophylline. It has been shown in cats²³ that the lethal dose of this theophyllinated genin is much larger than that which might be expected on the basis of the amount of genin used in its preparation. Changes in the ST segment appear in a far lower percentage of animals given the theophyllinated genin than those given digitalis. Such a drug may prove to be useful, but further experience will be necessary to determine its value in clinical practice.

The activity of digitalis, strophanthin and squill depends on the presence of an unsaturated lactone in the molecule. Recently Kraye et al.²⁴ showed that certain simple, synthesized, unsaturated lactones have a definite pharmacologic effect on the frog heart, producing an increase in amplitude followed by a period of diminished relaxation of the ventricle which terminates in systolic standstill.

Certain recent studies of the effect of digitalis on auricular fibrillation are of interest. In digitalizing patients with auricular fibrillation, one of the objects of therapy is to reduce the ventricular rate. It was shown many years ago²⁵ that patients with auricular fibrillation given ordinary therapeutic doses of digitalis would nevertheless show a much greater rise in pulse rate in response to exercise than normal persons of the same age group. This acceleration, which can be reproduced by the administration of atropine sulfate,²⁶ is the cause of considerable discomfort, shortness of breath and a sense of palpitation. Recently, however, evidence has accumulated^{26, 27} to show that this inhibition of the vagal effect on effort may be reduced by larger doses of digitalis. It is apparent that digitalis maintains a slow ventricular rate by the summation of two factors, one a

vagal factor abolished by atropine, the other an extravagal factor not abolished by atropine. In patients with auricular fibrillation and mild symptoms of congestive failure, it is advisable to digitalize to such a degree that exercise or emotion results in but a relatively slight increase in ventricular rate. The necessary dose may be quite close to that which induces impairment of appetite and nausea.

To summarize, it is incumbent on the physician to understand clearly the changes in the potency and dosage of the digitalis preparations in the light of recent developments. The variations that exist in dosage and potency of various preparations of digitalis make it advisable for the physician to utilize a single preparation with whose action and potency he is familiar. In a patient whose optimum maintenance dose is well regulated on one product, indiscriminate shifting to another preparation of different potency may lead to untoward effects. While certain purified crystalline preparations of digitalis possess the advantages of uniformity and obviate the necessity for bioassay, they possess no advantages over the *U.S.P.* powdered leaf or tincture in the treatment of the majority of patients. The increased cost of these preparations to the patient should be considered by the physician, since prolonged administration is usually necessary. In the unusual case where rapid digitalization is necessary, purified preparations such as Digitoxin are superior for rapid digitalization by mouth, and the other purified preparations previously mentioned are likewise suitable for intravenous administration. In all cases where rapid digitalization by mouth or parenteral therapy is employed, it is necessary to be certain that the patient has not received any digitalis preparations within the preceding ten or more days. If such preparations have been taken, the exact dose and strength should be ascertained. In the last analysis, clinical assay of any particular product must be done on the patient. Persons vary so greatly in their responses to and requirements of digitalis that one must look to the patient to determine the exact dose of digitalis.²⁸

EDEMA AND DIURETICS

The important considerations in the treatment of congestive failure are bed rest, digitalization, salt and water intake, and diuretics. Concerning the latter two, certain recent publications are of interest and practical import.

It is well known that the administration of sodium chloride will, under certain circumstances, result in clinical edema.²⁹ When the water changes affect chiefly the extracellular fluids, it has been

shown that the base simultaneously retained or lost is sodium.³⁰ There is, therefore, good reason for rigid restriction of sodium chloride in congestive failure. Schroeder³¹ has demonstrated that satisfactory diuresis, as evidenced by loss of weight, could be obtained in patients with congestive heart failure if the salt intake was maintained at 1 gm. or less daily. Conversely, with fluid intakes of 2500 cc. daily, no gain in weight occurred unless the salt intake was greater than 1 gm. daily. More recently, Proger et al.³² have demonstrated that the physical signs of congestive failure—edema, elevation of venous pressure, increase in circulation time and so forth—may be induced in cardiac patients if the salt intake is high enough. It is thus apparent that one of the advantages of the Karell diet is due to the fact that 800 cc. of milk contains approximately 1 gm. of sodium chloride. Diets containing less than this amount daily are generally inadequate in protein and therefore are to be used for only short periods of time. Nutritional edema not infrequently is overlooked in patients with congestive failure and is particularly prone to occur because of anorexia, albuminuria or frequent paracenteses. The loss of protein to the tissues when edema fluid is forming and the dilution of the blood protein consequent to the increase in plasma volume that occurs in congestive failure are likewise significant.³³ A diet containing 1 gm. of sodium chloride and an adequate amount of protein is shown in Table 1. This diet should be supplemented by vitamin B complex. Fluids may be allowed freely, except when renal failure is present.

Potassium chloride. In some patients, satisfactory diuresis may be obtained with a low-salt intake if potassium chloride is administered in doses of 3 to 5 gm. daily. This can be conveniently placed in a salt shaker and given to the patient to use with his low-salt diet.

Xanthines. Since the introduction of the mercurial diuretics, the use of the xanthines in the treatment of edema has been somewhat neglected. It must be stressed, however, that in many patients with congestive failure and slight to moderate amounts of dependent edema, satisfactory diuresis can be obtained and maintained by the oral administration of enteric-coated theobromine or theophylline sodium acetate. In some of these patients, attacks of cardiac asthma tend to occur whenever slight edema or latent edema occurs. The continued use of the xanthine diuretics under such circumstances may result in conspicuous improvement. Gastric symptoms are rarely encountered with these drugs except when doses in excess of 1 gm. four times daily are administered. Rise-

man and Linenthal³⁴ recently reported beneficial results in 2 patients with congestive failure who were treated for long periods of time with enteric-coated theobromine sodium acetate. In massive edema, however, the xanthines are of little value and mercurials or paracentesis or both must be utilized.

Urea. In refractory cases of edema, urea in doses of 60 to 90 gm. daily, in divided doses, may result in satisfactory diuresis.³⁵ The drug may also be used when mercurial diuretics are contraindicated, as in renal failure or acute inflamma-

persons, the danger of deposition of the mercurial agent in the fatty tissue and of resultant slough is obvious. The intravenous route may result in venous thrombosis. The rectal route, even when the suppositories are coated with a local anesthetic, occasionally results in marked inflammation and consequent pain and discomfort. To the ambulatory patient, therefore, an effective oral mercurial diuretic would be a boon. Calomel was the first mercurial preparation used for this purpose.⁴¹ However, diuresis following its use was often unsatisfactory and poisoning sometimes oc-

TABLE 1. *Sample Diet Containing 2000 Calories and 1.0 Gm. of Sodium Chloride.**

BREAKFAST		FOODS TO BE AVOIDED		FOODS TO BE USED FREELY (except for caloric content)	
1 orange or ½ grapefruit or ½ cup orange or grapefruit juice		All salted, brined, corned, pickled and smoked foods		Salad oils and fats (chicken fat, lard and so forth)	
Dark cereal — 30 gm dry (shredded wheat, oatmeal or enriched cream of wheat)		Salt, pepper and paprika		Sugar, syrups, jelly and candy	
Cream (20 per cent) — 120 gm		Bacon and ham		Arrowroot cookies	
Salt free butter — 5 gm		Meat soups, broths and gravies		Flour (in small amounts for cooking)	
Sugar		Shellfish			
Coffee		Milk, cheese (except cottage cheese) and ice cream			
LUNCH		Vegetables of high salt content, such as beets, celery, sweet potato and greens (including lettuce and spinach)			
1 egg or 30 gm cottage cheese		Bananas			
Almonds or rice — 30 gm dry (optional)		Crackers			
Enriched white bread — 1 slice (30 gm)		Molasses			
Vegetable — 100 gm serving (raw or cooked)					
Salt free butter — 15-30 gm					
Fruit — 100 gm serving					
Sugar or jelly					
Tea as desired					
DINNER		PERMITTED FRUITS (fresh or canned)		PERMITTED VEGETABLES (fresh or canned)	
Meat or fish or fowl — 120 gm (fish should be plain white fish, such as haddock or halibut)		Apple		Asparagus	
Potato (white) — 150 gm		Apricot		Brussels sprouts	
Vegetable — 100 gm serving (raw or cooked)		Blueberries		Beans (lima)	
Enriched white bread — 1 slice (30 gm)		Cantaloupe		Beans (string)	
Salt free butter — 30 gm		Cherries		Cabbage	
Fruit — 150 gm		Grapefruit		Carrots	
Cream (20 per cent) — 30 gm		Grapes		Cauliflower	
Sugar and coffee as desired		Lemon		Corn	
Potassium chloride, 3 to 5 gm, supplied in a salt shaker, may be added to this diet.		Peach		Eggplant	
		Pear		Onions	
		Pineapple		Parsnips	
		Raspberries		Peas	
		Rhubarb		Potatoes (white)	
		Strawberries		Pumpkin	
		Watermelon		Squash	
				Turnips	
				Tomatoes	
APPROXIMATE CONTENT		Calculation of this diet was based on tables in Stern's <i>Applied Dietetics</i> supplemented by figures from Patten's <i>Dietetics</i> (1940 ed).			
Carbohydrate	230 gm	Vitamin A	5800 I U		
Protein	60 gm	Vitamin B ₁	13 mg		
Fat	90 gm	Vitamin B ₂	11 mg		
Sodium chloride	1.0 gm	Vitamin C	100 mg		
Calcium	0.5 gm.	Calories	1970		
Phosphorus	0.96 gm				
Iron	0.011 gm				

*We are indebted to Mrs Marie Alexander for planning this diet.

tory conditions of the kidney or both. It is best given three times daily, immediately after meals, in ice-cold solution. The unpleasant taste may be masked by solution in syrups, such as acacia, or fruit juices. After several days of administration, the blood nonprotein nitrogen should be determined to ascertain whether the urea is being properly excreted. In almost all cases of congestive heart failure, however, the drug is readily excreted, carrying with it large quantities of water.³⁶

Mercurial diuretics. The action of the mercurial diuretics is directly on the kidney, causing diuresis by a reduction in tubular reabsorption of water.³⁷⁻⁴⁰ They may be administered intravenously, intramuscularly, rectally or orally. In obese

persons, the danger of deposition of the mercurial agent in the fatty tissue and of resultant slough is obvious. The intravenous route may result in venous thrombosis. The rectal route, even when the suppositories are coated with a local anesthetic, occasionally results in marked inflammation and consequent pain and discomfort. To the ambulatory patient, therefore, an effective oral mercurial diuretic would be a boon. Calomel was the first mercurial preparation used for this purpose.⁴¹ However, diuresis following its use was often unsatisfactory and poisoning sometimes oc-

increases the effectiveness of the oral preparation. Borg⁴⁵ has confirmed these results in a study of 39 patients, of whom 29 obtained a good diuresis. Toxic symptoms observed included nausea, vomiting, abdominal discomfort, pain and general weakness. In 3 cases, the drug had to be discontinued because of severe diarrhea; in the remainder, the symptoms were transient and the drug could be continued. No evidences of kidney irritation or of blood disturbances were noted. The oral dose recommended is 2 tablets three times daily at the beginning of treatment, with a reduction in the dose to an amount necessary to prevent reaccumulation of the edema.

Toxic reactions to mercurial diuretics. In the past several years, acute mercury poisoning and 27 deaths have been ascribed by various authors⁴⁶⁻⁵⁰ to the mercurial diuretics—Salyrgan, Mercupurin, and Esidrone. The toxic symptoms varied from slight dyspnea and orthopnea to syncope, pallor, shallow respiration and slow (20 to 30 per minute) pulse rates. In several cases, death occurred within one or two minutes after the injection was completed. Although in most cases the route of administration was intravenous, in at least 1 case toxic symptoms occurred after rectal administration. The mechanism of death due to mercurials in animals is mainly that of a direct toxic effect on the heart.⁵¹ Electrocardiograms show depression of the T waves, runs of extrasystoles, ventricular tachycardia and, terminaly, ventricular fibrillation. The incidence of such toxic symptoms must be extremely small, since although millions of doses have undoubtedly been administered, the number of deaths is few.

To summarize, rectal administration of the mercurials is frequently indicated and, except in extremely edematous or obese patients, the mercurials are better given intramuscularly than intravenously. If the drug is to be given intravenously, it should be diluted to 20 cc. and administered slowly. If given rectally, a small enema should precede the insertion of the suppository. The latter should be coated with an anesthetic ointment, such as nupercaine or pantocain. Although the possibility of mercury poisoning is slight, constipation should be prevented in patients receiving mercurials. It must be further remembered that many patients can be treated with xanthines after they have been rid of most of the edema fluid. In patients with considerable accumulations of edema fluid who have previously been digitalized, a marked diuresis may lead to the signs and symptoms of digitalis toxicity, which can readily be avoided by prior reduction in dosage. Christian⁵² has cautioned that in older men who have prostatic involvement it is wise to remember that an active

diuretic response may overdilate the bladder and precipitate symptoms of acute urinary obstruction. In this type of patient, constant catheter drainage during the stage of active diuresis may well be a prophylactic procedure that may obviate a forced prostatectomy.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANIE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

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CASE 28491

PRESENTATION OF CASE

First admission. A twenty-seven-year-old mill-worker entered the hospital for the first time because of pain in the right knee.

Two weeks before admission the patient developed an intermittent dull pain in his right thigh and knee, which was more severe on walking. One week later he began having two or three watery stools each day. Three days before entry he became constipated. He had not noted any blood or mucus in the stools.

Four years before entry he was operated on for acute appendicitis at another hospital, and tuberculous peritonitis was found; the appendix was removed. He had had no subsequent symptoms.

Physical examination showed a well-developed, undernourished man complaining of pain in the knee. Examination of the heart and lungs was negative. In the right flank was a hard, fixed, nontender mass about 5 cm. in diameter. The right knee was painful on extension, but no definite cause could be discovered.

A barium enema showed that the cecum was irregular in outline and immovable. At the end of six hours the cecum was incompletely visualized. A chest roentgenogram was negative. In view of his past history, a presumptive diagnosis of tuberculous of the cecum was made, and he was sent to a sanatorium.

Second admission (twelve years later). He remained in the sanatorium for fourteen months, during which period his weight increased from 110 to 170 pounds. He was seen in the Out Patient Department of this hospital three years after his discharge from the sanatorium; he appeared very well, was free from symptoms and was able to do heavy work. He was examined four years later and was still in excellent health.

Four weeks before re-entry, — the patient was then thirty-eight years old, — he was seen in the Out Patient Department because of a lower abdominal ache and urinary frequency of two weeks' duration. Cystoscopy revealed "whitish specks" scattered over the bladder mucosa which were suggestive of chronic cystitis. The urine showed

a very slight trace of albumin, and the sediment contained 2 to 4 white cells and large clumps of bacteria per high-power field; culture revealed only a few colonies of *Staphylococcus albus* and diphtheroids. Two days later he developed a pain in the right flank, which radiated around into the right lower quadrant. Roentgenograms of the abdomen showed an area of bony condensation close to the right sacroiliac joint, that did not shift in position in various films. An intravenous pyelogram showed prompt excretion of the dye on both sides; on the left, the kidney pelvis and ureter were normal, but on the right, there was slight but definite dilatation of the kidney pelvis and of the upper half of the ureter down to the area of condensation described in the bone. Because of the organisms found in the urine culture the patient was treated with methenamine. Two weeks before entry he gradually began to feel weak, and occasionally had cold sweats and shaking chills at any time of the day. He often vomited half an hour after eating; no blood or coffee-grounds material was noted. He continued to have daytime frequency without hematuria, and nocturia three or four times. He denied dysuria, urgency, incontinence, dribbling or the passing of urinary stones. At the time of admission he was very uncomfortable because of a dull ache in the right flank and right inguinal region and because of inability to retain food. During the four weeks of illness he had lost 22 pounds. He denied any change in bowel habits but stated that four weeks before entry he had passed a small amount of fresh blood just once.

The family history was noncontributory. The patient had lived in Massachusetts all his life and worked as a wool carder.

Physical examination revealed a well-developed but tired-looking man who was moderately uncomfortable. He belched frequently. A few small nontender lymph nodes were felt in each groin. Examination of the lungs and heart was normal. In the right lower quadrant just to the right of the midline there was slight fullness, and just above the inguinal ligament a poorly outlined, hard, fixed, tender mass about the size of a grapefruit, which was dull to percussion. No other masses were felt. There was constant pain in the right costovertebral angle on deep pressure. On rectal examination the mass in the right lower quadrant was felt.

The blood pressure was 130 systolic, 85 diastolic. The temperature was 101.6°F., the pulse 90, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,750,000 with a hemoglobin of 80 per cent and a white-cell count of 22,500 with 90 per

cent polymorphonuclears. The urine was acid in reaction, had a specific gravity of 1.015 and gave a + test for albumin; the sediment contained 5 red cells and 25 white blood cells per high-power field. When repeated, no proteinuria was found, and only an occasional red blood cell and white blood cell were seen in the sediment. The stools were loose, and one stool examined for blood was negative. The nonprotein nitrogen was 24 mg., and the total protein 5.5 gm. per 100 cc.; the blood chloride was 99 milliequiv. per liter.

A flat plate of the abdomen showed an ill-defined soft-tissue mass pressing on the air-filled cecum. There were several slightly dilated air-filled loops of small intestines seen in the right side of the abdomen. The distention was not very marked. The psoas shadows were clearly visible. The upper portion of the right sacroiliac joint was poorly outlined and less dense than that on the left. An x-ray film of the chest revealed that the right diaphragm was slightly high in position. There was no evidence of fluid. The lung fields were clear.

On the day after admission the patient's temperature rose to 104°F., and two days later he had a chill, after which the temperature rose to 103.4°F. Vomiting continued during hospitalization, and loose watery stools occurred each day. On the fourth day after admission the abdominal mass seemed larger and the abdomen was more distended. There was increased spasm of the abdomen, particularly on the right.

An operation was performed on the fourth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM B. BREED: There are three approaches here—three points of view that one might take. One is that the etiology of the patient's illness over a period of more than twelve years is the same. Another point of view is that there were two entirely separate episodes in his medical career; the third is that there may have been some mechanical defect produced during the first illness which may have complicated the final outcome.

Let us examine the first thesis, to see if it is reasonable to suspect that this was all due to one cause. We see that a presumptive diagnosis of tuberculosis was made. I should like to know who made the diagnosis of tuberculous peritonitis four years previously when he was operated on for appendicitis. I think that the observation must be established as a correct one before one can even make a presumptive diagnosis of tuberculous cecum. Moreover, my impression is that tuberculous peritonitis and colonic tuberculosis are not

often seen in the same patient. Is that correct, Dr. Holmes?

DR. GEORGE W. HOLMES: I do not believe I am competent to answer that question.

DR. BREED: Does one find tuberculous peritonitis often in the presence of gastrointestinal tuberculosis?

DR. HOLMES: I should say not.

DR. FLETCHER H. COLBY: We have had several patients lately who have had tuberculous lesions of the small and large bowel, and none of these have had tuberculous peritonitis.

DR. BREED: That is my impression, but my experience is not very broad. What would you say, Dr. Mallory?

DR. TRACY B. MALLORY: I think your statement is true.

DR. BREED: He may have had tuberculous peritonitis. We have often been told that exploration clears up the peritonitis, but I have never been very convinced that that is true. Also, I should like to cast some doubt on the diagnosis of peritonitis of tuberculous origin. I should also like to ask the roentgenologist if he was sure that the patient had tuberculosis of the cecum. Would you be willing to look these films over now, Dr. Holmes?

DR. HOLMES: They are not here; they were destroyed.

DR. BREED: The trouble is, that when the patient came in the second time, no observation was made on the cecum or colon by barium so we do not know if he had a defect in his cecum—he may have been too sick for such an investigation. All we have at the last admission is the flat plate.

Of course anybody going to a sanatorium and sitting around in the sun gains weight and feels better, and the fact that the patient got well does not really decide the question whether he had tuberculosis. At the time he came in with a sore knee and they were making a presumptive diagnosis of tuberculosis, they did not take an x-ray film of the knee; so that leaves us in the dark. There are no x-ray films here? Although no x-ray films were taken, it was thought that he had tuberculosis of the knee or hip.

DR. HOLMES: From the description of the examination of the colon at that time it is suggested that the cecum was spastic. This is usually seen in ulcerative tuberculosis. The ulcerative type is usually accompanied by some pulmonary lesion, which the patient did not have.

DR. BREED: I am about to cast considerable doubt on the diagnosis of tuberculosis of the cecum. Although he had had pain in the right flank previously and also had a rather sudden onset of right flank pain on the second admission, he had been

so well during the intervening twelve years, and able to do heavy work, that I am rather inclined to think these were two separate episodes and that there was no common etiology. I shall take that stand.

Concerning the third point of view that I mentioned, whether there was some defect on which this infection was superimposed, I have as yet no opinion.

Have we any x-ray films taken during the second admission? Will you tell me something about the bony condensation and so forth?

DR. HOLMES: Apparently, these films were all taken at about the same time. Certainly the chest shows no evidence of tuberculosis. The diaphragm is a little high on the right, but that does not strike me as being remarkable. The liver shadow is large rather than small, but not definitely outside normal limits. I suspect the patient had a little enlargement of the liver. So far as the urinary tract is concerned, I can see the pelvis of the kidney on the right side very well. The fact that that remains filled and the whole ureter remains filled and the other side empties, suggests an obstruction of the ureter. That is the only concrete finding. The dilatation is certainly very slight. The statement of condensation in the bone does not impress me at all. I do not see anything that I would be convinced was abnormal. I do not know what they meant.

DR. BREED: It did not mean anything to me.

DR. HOLMES: It is an unusual term.

DR. BREED: And moreover, it is not there, whatever it is.

DR. HOLMES: That is right. Apparently the patient had a marked dilatation of the small bowel. A Miller-Abbott tube was inserted, and this film was taken to show the position of the tube. There is a good deal of gas, and I do not believe it is confined to the large bowel. There is some in the small bowel, and a moderate degree of dilatation.

DR. BREED: Have you a flat film showing the soft-tissue mass in the flank?

DR. HOLMES: This might be the mass outlined by the gas in the colon.

DR. BREED: The sacroiliac joint is not diseased, but there is perhaps obstruction to the ureter—partial, not complete.

Would you please, Dr. Colby, interpret for me the statement, "Cystoscopy revealed 'whitish specks' scattered over the bladder mucosa, which were suggestive of chronic cystitis"? Was there any suggestion of tuberculosis?

DR. COLBY: It means very little to me. From this description there is nothing in the bladder that is typical of tuberculosis. In the first place, there were no ulcerations, and in the second place,

there is no description of the so-called "submucous tubercles," which are red areas with tiny white centers. The whitish specks could perfectly well be particles of exudate adherent to the bladder mucous membrane—that is all.

DR. BREED: I might say from reading this over that this man had a urinary infection. One sediment showed a few white cells but one showed nothing. Of course he could have had infection with an obstructed ureter on the right, without showing anything in the urine. That brings up a question we have to decide, that is, whether the lesion was in the gastrointestinal tract or in the urinary tract. That is my problem.

DR. COLBY: I think it is fair to assume that the patient had some urinary-tract infection because he had pus in his urine on at least two examinations and a positive culture. I do not know how the urine was taken; only a few *Staph. albus* colonies were found, which might be contamination or might mean something.

DR. BREED: Have you ever seen an abscess in the cecal region originating in the gastrointestinal tract that might produce, by spasm, some obstruction to the ureter like this?

DR. COLBY: Yes

DR. BREED: It is reasonable to expect that, if there was an inflammatory mass in this region, the ureter would not empty normally?

DR. COLBY: A tumor or an appendix abscess will cause an obstructed ureter and hydronephrosis.

DR. BREED: That is what I am driving at, and it leads me to the conclusion that I had already come to, and had hoped to keep prominent, namely, that the lesion was probably not in the urinary tract but in the gastrointestinal tract.

If it was in the gastrointestinal tract, what kind of lesion was it? From all I can read here it seems to have been an abscess. The patient had chills, fever and a tender mass extending from the flank down to the right lower quadrant, with a white cell count of 22,500 and 90 per cent polymorphonuclears. He presented the so-called "acute surgical belly." Someone operated on him. I assume he was operated on by an abdominal surgeon and not by a genitourinary surgeon. It might have been difficult to decide what surgeon one would choose. I shall pick the abdominal surgeon. I think he operated and found some sort of abscess.

What was the source? It still is possible for the patient to have had an appendiceal abscess. The stump may not have been buried fourteen years previously and he still might have had some infection lurking there which flared up into an ab-

success. The story is a pretty good one for it. I admit that the time element is a long one.

I do not believe it is tuberculosis for reasons that I have already discussed.

Could the patient have had regional ileitis? He could and might have had regional ileitis.

Could he have had a retroperitoneal abscess? If so, what was the source of it? I cannot imagine.

I shall predict that the patient was operated on by an abdominal surgeon who found an abscess, the exact source of which I cannot designate and that he very likely got well and did not have any underlying pathologic lesion, such as cancer or lymphoma, in spite of the fact that small, non-tender lymph nodes were noted in each groin. We find such nodes frequently, and it does not disturb me. No tuberculosis, no cancer, no lymphoma—a pyogenic infection in the peritoneal cavity in the region of the cecum, the source of which is unknown. The patient may have had regional ileitis that perforated—but that diagnosis cannot be made.

DR. WILLIAM A. BISHOP: Examination of the right lower quadrant showed evidence of an old healed sinus. Is that to be connected? I saw him in the Out Patient Department. He had evidence of an old healed sinus in the region of the cecum.

DR. BREED: He had had appendicitis. Why do you say "healed sinus" rather than "healed scar"?

DR. MALLORY: There was a history that the sinus had drained for some months at the Lakeville Sanatorium. That should have been in the hospital record.

DR. BREED: I think it certainly should! The history of a draining sinus in a patient who had been in a tuberculosis sanatorium makes quite an impression on me.

DR. BISHOP: It did on me. That is why I sent him to the hospital.

DR. BREED: How often does one see a draining sinus with tuberculosis of the cecum?

DR. ROBERT R. LINTON: That has not been operated on?

DR. BREED: He had his appendix out.

DR. LINTON: I think it is not uncommon to see it immediately after appendectomy with a tuberculous cecum, but it is a little surprising that it healed if it was tuberculous.

DR. BREED: Even in a sanatorium?

DR. LINTON: Yes.

DR. BREED: But it did heal!

DR. BISHOP: And how do you account for the thigh and knee pain?

DR. BREED: I give up—no one was interested in it. They did not even x-ray the hip or knee.

DR. BISHOP: How about psoas irritation or abscess?

DR. BREED: Possibly psoas abscess; but the x-ray films show that the psoas muscles were clear.

DR. MALLORY: The sinus would be at least equally in favor of regional ileitis.

DR. LINTON: I think that is true, and such a sinus would be likelier to close up than a tuberculous sinus.

CLINICAL DIAGNOSIS

Intraperitoneal abscess.

DR. BREED'S DIAGNOSIS

Peritoneal abscess in region of cecum (pyogenic—? source).

ANATOMICAL DIAGNOSES

Malignant lymphoma, clasmatocytic type, of mesentery, involving ileum, cecum and sigmoid.

Ileosigmoidal fistula.

Retroperitoneal abscess.

Appendectomy wound, healed.

• Sinus tract, healed.

Cystitis, slight.

• Pyelonephritis, right, slight.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This man was explored, and a huge tumor mass consisting mostly of enlarged retroperitoneal lymph nodes with obvious extension to several loops of bowel was found. A biopsy was taken, and the surgeon backed out as quickly as he could. Biopsy showed a malignant lymphoma of the reticulum-cell or clasmatocytic type. The patient went downhill very rapidly and died. At autopsy, we did find Dr. Breed's abscess in the retroperitoneal tissues.

DR. BREED: Thank you.

DR. MALLORY: That had not been found by the surgeon. There was a huge tumor mass, chiefly in the mesentery, which had invaded the cecum, a portion of the ileum and a portion of the rectosigmoid. There was a fistulous opening between the ileum and rectosigmoid so that the large bowel was entirely short-circuited. The liver contained many metastases, but the other organs—the spleen, lungs, kidneys and so forth—were free from metastasis. There was a mild grade of cystitis.

DR. BREED: Do you think the episode twelve years ago had anything to do with the last one?

DR. MALLORY: I think not. We found no evidence of tuberculosis at autopsy.

DR. HOLMES: Was the liver large?

DR. MALLORY: Quite, it weighed 2300 gm.

DR. BREED: Were the inguinal lymph nodes positive?

DR. MALLORY: No; they did not contain tumor.

CASE 28492

PRESENTATION OF CASE

A fifty-nine-year-old chauffeur came to the hospital because of diarrhea.

Approximately six months prior to admission he was first bothered by "gas," which usually occurred a short time after meals and was partially relieved by soda and ginger. Three months later a dull pain developed just below the umbilicus. His physician prescribed pills, but these were ineffectual in providing relief. Despite the pain the patient was able to work without great difficulty. During the illness his bowels moved regularly without cathartics. Five weeks before entry, because he was slightly constipated, he took a Scidlitz powder in the morning, and since there was no bowel movement, he repeated the dose several hours later. Soon after the second dose he began to have a loose bowel movement, and the diarrhea persisted up to the time of entry. With the onset of diarrhea the abdominal pain was relieved and did not recur. The diarrhea usually developed several hours after meals, but was most bothersome at night. It often occurred two or three hours after supper and lasted four or five hours. He believed that ingested fluids were evacuated twenty to thirty minutes later. With the onset of diarrhea the feces became very foul smelling but were never tarry or bloody. He had had rare attacks of cramps and said that his stomach "rolled" a great deal. During the five weeks prior to admission he had lost 15 to 18 pounds.

The family and past histories were noncontributory.

Physical examination revealed a well-developed and well-nourished man who appeared to be in good health. Examination of the lungs, heart and abdomen was negative.

The blood pressure was 126 systolic, 80 diastolic. The temperature was 97.8°F., the pulse 70, and the respirations 16.

The examination of the blood revealed a red-cell count of 4,100,000 with a hemoglobin of 11.5 gm. per 100 cc. The urine was normal. The stools showed a + guaiac test. The blood Hinton test was negative. The serum nonprotein nitrogen was 34 mg. per 100 cc., and the protein 5.8 gm. A barium meal and enema demonstrated a fistula between the third portion of the duodenum and the proximal third of the transverse colon.

An operation was performed on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD SCHIATZKI: It is easy to summarize the highlights of this history by saying that this was a patient with constant diarrhea of five weeks'

duration, during which period he had lost some weight. The diarrhea was superimposed on a six months' story of indigestion. X-ray examination demonstrated a fistula between the proximal transverse colon and the third portion of the duodenum.

In addition to the short x-ray description in the case history I have been given films taken in an outside hospital. These apparently represent two examinations—a barium enema, and a gastrointestinal series that was done on the following day. There is something wrong with the report in the record. It is obviously impossible that the patient could have had a fistula between the transverse colon and the third portion of the duodenum because these portions of the bowel never touch, at least not in this case. I suppose what the fluoroscopist meant was a fistula between the proximal transverse colon and the lower part of the second portion of the duodenum. At least the roentgenologist took a spot film over the area that he thought was the site of the fistula, and it corresponds to the area that I have just mentioned. On all these films taken during the enema the duodenum is filled apparently from the colon. And on the gastrointestinal series taken the next day the transverse colon is filled. The proximal transverse colon and the lower part of the descending duodenum are constantly in close proximity in all the films so that establishes the possibility of a fistula in this area. If there is a supposed fistula, one studies the area very carefully and looks for further abnormalities. In this respect, the films are very disappointing. The film of the colon shows no defect, and the duodenum in the area of the fistula appears normal. However, the reading of x-ray films of the gastrointestinal tract in patients whose fluoroscopy was done by someone else is a highly unreliable practice, and most radiologists abhor it. But I have to take what I get in this case.

Beyond the demonstration of a fistula, the existence of which we had already surmised from the history, the films do not give us any information. I might mention this small diverticulum in the third portion of the duodenum. I am sure it is irrelevant, however.

This patient supposedly had a spontaneous fistula between the proximal transverse colon and the second portion of the duodenum. What can cause such a fistula? I shall start by saying that this kind of fistula is much less common than one between the stomach and the colon; but it does occur and not too infrequently, and the usual cause is a cancer of the hepatic flexure of the colon. We have no evidence of such a cancer in these films and therefore have to throw out this commonest cause. As soon as we do this, we are confronted

with rare things. A cancer of the duodenum has been described as causing perforation into the colon, but we have no evidence of such a cancer. I can conceive of a neoplasm on the outside of the two organs perforating into both of them, but there is no evidence of such a lesion. The retroperitoneal structures are perfectly normal. I can conceive of a gallstone that had perforated into the colon and at the same time into the duodenum, thus forming an inflammatory mass that communicates with the colon and establishes a fistula between the three places. In such a case one would expect to see some air in the bile ducts; since I do not see it, that is out.

What remains is a very rare possibility, that of perforation of a benign peptic ulcer of the second portion of the duodenum. The history is suggestive. The patient had had symptoms for several months and was relieved by soda. The abdominal pain stopped very suddenly, and from then on he had diarrhea. This is almost a classic story of what happens in patients with marginal ulcer that secondarily results in the formation of a gastroduodenocolic fistula. The ulcers are very rare, but very occasionally a fistula in such a case has been described. I know of only two such cases in the literature. The most convincing one was described by Dr. C. N. McPeak,* of Fitchburg. Against such a diagnosis is the fact that we do not see any intrinsic bowel lesion in the area of the fistula. There is no induration of either the colon or duodenum. For want of a better explanation I should put this explanation first, but before concluding I must mention another possibility. When a fluoroscopist gives a barium enema, he does not usually see the barium go through the fistulous tract into the duodenum or stomach. He suddenly finds barium where it should not be and then traces it backward but does not necessarily find the place of the actual fistula. In other words we must consider the possibility that the fistula was not in the area that was examined and was lower down, somewhere beyond the ligament of Treitz. In such a case, carcinoma, or possibly lymphoma, is the commonest cause. Extremely rare cases of benign peptic ulcer of the jejunum have also been described, but this area is poorly visible on the films I have here. I cannot go beyond mentioning a fistula below the ligament of Treitz as a possibility. Certainly if someone brought these films to me with this report from an outside roentgenologist and said, "Shall I operate?" I should say, "Let me fluoroscope first."

A PHYSICIAN: I should like to ask Dr. Schatzki if a diverticulum of the duodenum can produce such a picture.

DR. SCHATZKI: I do not believe that a simple diverticulum can do it—unless something happens to it, that is, it becomes occluded by a foreign body. That is a possibility.

DR. WILLIAM B. BREED: I should like to ask Dr. Schatzki if he is willing absolutely to rule out cancer because he cannot see evidence of it by x-ray.

DR. SCHATZKI: If I had fluoroscoped this patient myself and was convinced that the intestine on both sides of the fistula was normal, I should exclude it. Just looking at the films I should have to make that restriction.

CLINICAL DIAGNOSIS

Duodenocolic fistula.

DR. SCHATZKI'S DIAGNOSIS

Ulcer of duodenum, with duodenocolic fistula.

ANATOMICAL DIAGNOSIS

Adenocarcinoma of colon, with jejunocolic fistula.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Only the expert is acutely aware of the potential pitfalls of his technique. Dr. Schatzki was justifiably suspicious of the accuracy of the localization of the fistula and suggested that it might even be below the ligament of Treitz. If he could have been sure of this point he would have made a diagnosis of some form of malignant disease. At operation it was found that the fistula was actually some 15 cm. beyond the ligament of Treitz and connected the jejunum with the transverse colon. A large tumor mass involved all layers of the walls of the jejunum and the colon, with craterlike ulceration of the mucosa in each segment of the bowel. So far as the gross appearance was concerned, it could have been primary in either organ. It proved to be an adenocarcinoma, which gets us no farther, and we are forced back on the law of chances in attempting to decide where it was primary. Cancers do occur very exceptionally in this portion of the jejunum, and it is conceivable that it was primary there. On the other hand the chances are 1000 to 1 that it was primary in the colon.

DR. SCHATZKI: This case supplies the answer to a question that always arises when a patient has been fluoroscoped in an outside hospital. The question is, Should the patient be fluoroscoped again? We try to save the patient money and go ahead with the operation, but we should not do so, unless the findings are very obvious. We should fluoroscope again.

DR. MALLORY: Certainly it would have been worth while in this case.

*McPeak, C. N. Benign duodeno-colic fistula: with report of 2 cases. *Radiology* 34:343-350, 1940.

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"THE MEDICAL CURRICULUM"

THERE is much mental food in an editorial under this title in the August 15 issue of the *British Medical Journal*. One senses that medical educators in England have been as violently disrupted in their thinking as in their physical plants and activities, but that they are beginning to pull themselves together and to look into the dark corners now illuminated by the wartime searchlights. One also senses that great and inevitable changes in the training of physicians are close at hand. A system that has been dominated by scientific investigators and successful consultants is producing too few general practitioners; it must turn back and concern itself more intimately with the knowledge and bodily skills required by the practicing

doctor. At the same time, it might acquire some of the methods of selection and training that have so markedly accelerated the acquisition of industrial skills during the war. The application of these changes should be integrated with a social and economic structure that will permit young men and women to marry freely at the age of twenty-three or twenty-four years; otherwise, the best stock may tend to be bred out of the race. Thus, the writer develops a rough outline of what the future British medical curriculum should provide for.

This startling revelation about medical education in Britain applies as well to the United States. Recent and present graduates are finding themselves in a world whose ideals and demands are proving very different from those of the schools in which they were trained. Often, the information they most urgently need was not emphasized in their undergraduate courses. The historical, and on that account obscure, fact that smallpox can be prevented by inoculation, for example, might these days become a primary piece of knowledge in an island garrison. The neglect of preventive opportunity of any sort will soon cease to be an omission; it will become an error of commission. Graduates in army practice will wonder why they were not taught this in medical school. The lungs with cavities, the livers with lumps and the various advanced degenerations of the retina may still provide teaching material, but they are not the stuff of which medical practice has been or will be made. They are the gross, the rare, the allegedly interesting, and contrast sharply with the trivial but common deviations that occupy most of the practitioner's time. As time goes on, the practitioner will want to know less about the museum and more about the conditions under which men should live, eat, sleep, work, love and play. How can they be taught to appraise these things?

How indeed? Certainly not by changing the curriculum, although that may well accommodate itself to the interests and activities of those who are currently responsible for it. The world of to-

day is moving into the hands of those who are active, dynamic, decisive—the “motor minds.” These people have always eschewed the deliberative, scholarly and somewhat cautious impulses that have built the academic past. As they now come into power, they may well change the facets of the medical-school curriculum, and polish them too, but whether the product can thereby be changed is another matter.

The constitutional pattern of a person may be either in harmony with or antagonistic to the environment in which he is called to function, and his performance consequently may be good or poor. Or more happily, he may possess an adaptable constitution, which will allow him to function well under a variety of conditions; this has always been the constitution of the good general practitioner, and has proved to be his great value in war. Britain has repeatedly called for general practitioners, not for specialists. An improved selective process, or series of processes, by which such persons could be screened away from the brilliant performers in narrow fields would make the greatest contribution to our systems of premedical and preclinical schooling. If it could have been applied to the prewar student body, there would be less indication for postwar revision of the medical curriculum.

VENEREAL-DISEASE CONTROL AND THE PHARMACIST

SINCE the passage of the Venereal Disease Control Act in 1938, the importance of the pharmacist as a factor in the control of venereal disease has achieved increasing recognition. This is to be expected because the pharmacist is often the first to be consulted by those who have, or suspect they have, a venereal disease.

The physician-pharmacist relation, which has existed in this country for many generations, is more than a mere tradition—it is a natural outgrowth of the close interdependence between physician and pharmacist in a common endeavor, namely, the healing of the sick. Thus both the

pharmacist and the physician bear a joint responsibility to society—to the people whose well-being depends greatly on their intelligent co-operation. The war effort has pointed up the individual responsibility of these allied health forces and, at the same time, has strengthened their interrelation in the united drive against diseases that sap the national strength.

Foremost among national health problems are the venereal diseases, which in World War I caused seven million days lost from service in the United States Army. As for the population generally, over 2 per cent of all persons have or have had syphilis. Although the actual prevalence of gonorrhea is not known, it is estimated that it strikes from three to seven times as often as syphilis.

A nationwide effort to eradicate syphilis and gonorrhea through a program of effective control is being co-ordinated by the United States Public Health Service. With funds appropriated by Congress and by state, city and county health departments, full-time professional workers have instituted vigorous health measures for the control of venereal disease. But no health-control project can be termed effective without the aid of the pharmacist.

The pharmacist himself is more aware than anyone else of his responsibility to the community in assisting the health authorities in the urgent task of bringing venereal-disease patients under proper treatment. A recent comment from the Public Health Service, published elsewhere in this issue of the *Journal*, emphasizes this responsibility. Through his professional organizations, notably the American Pharmaceutical Association, and with the co-operation of the American Social Hygiene Association, the pharmacist has demonstrated a willingness to take an active part in the national program for the control of syphilis and gonorrhea.

By participating in the program for venereal-disease control being promoted by the Public Health Service, by the state health authorities and by the Joint Committee of the American Social Hygiene Association and the American Pharmaceutical Association, the pharmacists of this coun-

try will strengthen public confidence in their profession. At the same time they will know personally that their efforts are being given toward the elimination of the venereal-disease scourge, both for the best interests of the civilian population and for the greater fighting efficiency of the armed forces of the Nation.

MEDICAL EPONYM

SIMMONDS'S DISEASE

The first reported case of hypophyseal cachexia was described by Professor Morris Simmonds (b. 1855) of St. George's General Hospital at Hamburg before the Medical Society of Hamburg on January 5, 1914. The paper was printed under the title, "Ueber Hypophysisschwund mit tödlichem Ausgang [Destruction of the Hypophysis with Fatal Outcome]" in the *Deutsche medizinische Wochenschrift* (40:322, 1914). A portion of the translation follows:

... The history of the illness is briefly as follows: A previously healthy woman suffers with severe puerperal sepsis. She develops a septic necrosis of the pituitary body. As a result of the loss of this vital organ there develop grave deficiency phenomena: menopause, muscular weakness, vertigo and attacks of loss of consciousness, anemia, rapid aging—in short, a "senium praecox." The remaining intact fragments of the gland gradually atrophy, being surrounded by connective tissue. The organ becomes entirely insufficient, and the woman dies in coma. Autopsy shows as the sole cause of death an almost complete disappearance of the hypophysis.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

HEMORRHAGE

Thirty-one maternal deaths that occurred in Massachusetts during 1941 were attributed to hemorrhage; in 16 of these, the hemorrhage was post partum, in 8 it was due to a separated placenta, in 5 to a placenta previa, and in 2 to a placenta accreta.

Of the 16 cases complicated by post-partum hemorrhage, the first was that of a multipara who had had five normal pregnancies. She began to bleed one hour after delivery of the placenta; the uterus was packed, and 2000 cc. of blood was administered. Ecchymotic spots developed all

over the body, and death occurred several hours post partum. In such a case the question of incompatibility always arises.

In the second case, that of a primipara who had had no prenatal care, bleeding occurred one week before delivery and had been preceded by a fall from a bicycle. Delivery was accomplished at home at about seven and a half months. Bleeding continued after delivery of the placenta; transfusion was not given, and death resulted one hour after delivery, before the patient could be transported to the hospital. In view of the fact that bleeding occurred at intervals after the patient's fall, it is possible that this fall in some way separated enough of the placenta to cause premature labor. The baby lived.

The third patient was a primipara who delivered herself spontaneously and began to bleed profusely eighteen hours post partum. Examination showed that the bleeding was coming from the vaginal mucous membrane. There was no bleeding from the uterus, which was hard, but there was a general oozing, which before death was complicated by bleeding from the rectum. Four transfusions were given. This was a very unusual case: the patient had syphilis and had received antisyphilitic therapy up to one month before delivery.

The fourth case was that of a multipara who was not seen until she was in labor. She was delivered at home, and the physician left shortly afterward, saying that everything was all right. The patient was left entirely alone, there being no one else in the house; a neighbor called in the evening and found her dead. This was undoubtedly a severe post-partum hemorrhage, although the death certificate attributed the fatality to "cardiac disease."

The fifth patient was a multipara who was delivered by simple low forceps. The placenta did not come away spontaneously, and one and a half hours after delivery profuse hemorrhage occurred. The placenta was removed manually shortly afterward, and a transfusion of 600 cc. of blood was given, in spite of which the patient died six hours later, undoubtedly from post-partum hemorrhage and shock. Additional transfusions might have averted this fatality.

The sixth case was that of a patient who had had intelligent prenatal care and in whom, after a spontaneous delivery, the uterus relaxed and did not regain normal tone. Death occurred two and a half hours after delivery.

The seventh case was that of a multipara who, following simultaneous delivery of the baby and placenta after a very strenuous labor, proceeded to flow freely and died in spite of the administration

of pituitary extract and ergotrate, and packing of the uterus. This death occurred at home; no transfusion was attempted.

The eighth patient was a primipara with a history of pulmonary tuberculosis who had a normal labor and began to bleed after delivery. The placenta was removed manually and is said to have been adherent. Five hundred cubic centimeters of blood was given, but death resulted in spite of this. It is possible that an additional transfusion should have been given and that a hysterectomy should have been considered.

The ninth patient, having had one previous uneventful pregnancy and convalescence, began to bleed two and a half hours after delivery, when she was found in a pool of blood. In spite of a transfusion, death occurred eight hours later. Massive hemorrhages do occur from atony of the uterus as late as two hours after delivery when there has been no previous unusual bleeding, but they are fortunately not common. Evidently much more blood than could be replaced by a single transfusion was lost before hemorrhage in this patient was recognized.

The tenth patient was a primipara who was delivered at home by mid-forceps after a seventy-two-hour labor. Hemorrhage followed delivery of the placenta and was checked by packing the uterus, but death occurred shortly. The patient was not given a transfusion. Such disasters are likelier to occur, of course, in a home than in a hospital, where the facilities for immediate transfusion should always be available.

The eleventh case was that of an elderly primipara in a hospital who, after delivery by low forceps following a normal labor, began to bleed after the birth of the placenta. The uterus and vagina were packed, but the bleeding continued. No transfusion was given, and the patient expired about five hours after delivery. There is hardly any excuse for a patient's dying of post-partum hemorrhage in a hospital.

It is difficult to ascertain the cause of hemorrhage in the twelfth case. Labor was induced in this patient for no apparent reason; after the cervix had become dilated to admit three fingers it was further dilated manually and the baby, which lived a few hours, delivered. The patient bled freely following delivery and went into shock, death occurring about one hour post partum. There is a possibility that the uterus was ruptured. This probably is a fatality attributable to bungling obstetrics.

In the thirteenth case, delivery was accomplished by low forceps in a patient who apparently had toxemia, and was followed by excessive post-partum hemorrhage. The vagina was packed and

the patient was transfused, but death occurred two hours after delivery. This patient had had ten previous spontaneous labors, and death was undoubtedly due to extensive post-partum hemorrhage.

The fourteenth patient was a multipara who had had three deliveries by cesarean section. When nearly at term she entered the hospital because of vaginal bleeding, and a cesarean section was immediately performed. Fifteen hours after delivery a profuse post-partum hemorrhage occurred; four transfusions were given, the uterus and the vagina were packed, but death occurred six hours later. One wonders why hysterectomy was not considered.

The fifteenth case was that of a patient on whom an elective cesarean was performed. Death occurred four and a half hours after the operation, and although the death certificate gives embolism as the probable cause of death, investigation leads one to infer that post-partum hemorrhage was the more reasonable diagnosis.

The sixteenth and last case in this group was a primipara who entered the hospital two hours after delivery. The placenta was extracted manually, presumably because of excessive bleeding, and the uterus was packed. In spite of this, bleeding continued through the pack, and hysterectomy was resorted to. Death occurred from peritonitis one week after delivery. Although this death was caused by peritonitis, the real reason for the operation was hemorrhage, and the case is so classified.

(To be concluded)

DEATHS

COCHRAN — WILLIAM J. COCHRAN, M.D., of Natick, died August 29. He was in his eighty-first year.

Dr. Cochran received his degree from Harvard Medical School in 1887. He was a member of the Massachusetts Medical Society and the American Medical Association and was formerly chairman of the board of health of Natick. He was a trustee of the Leonard Morse Hospital.

KEELEY — THOMAS H. KEELEY, M.D., of Monson, died August 28. He was in his forty-ninth year.

Dr. Keeley received his degree from the Middlesex University School of Medicine in 1923. He was a fellow of the Massachusetts Medical Society and the American Medical Association. He was on the staff of the Wing Memorial Hospital, Palmer.

WAR ACTIVITIES

CIVILIAN DEFENSE

INDUSTRIAL-HEALTH BROADCASTS

The two following series of industrial-health broadcasts will be given under the auspices of the Massachusetts Committee on Public Safety over the Boston stations indicated:

WMEY—Monday evenings, 10 10-10 15

- December 7 *Tuberculosis in Industry* Alton S Pope, M D
 December 14 *The Industrial Doctor* Louis R Daniels, M D
 December 21 *The Industrial Nurse* Catherine R Dempsey, R N
 December 28 *Industrial Rehabilitation* Daniel L. Lynch, M D

WNAC—Saturday afternoons, 12 30-12 35

- December 5 *Newer Chemical Hazards in Industry* John P Fahy, A B
 December 12 *Hazards to Health in Making Munitions* Irving R Tabershaw, M D
 December 19 *Industrial Skin Diseases* George E Morris, M D
 December 26 *Radium Poisoning among War Workers* W C L Hemen, S M

The speakers in the first group are members of the Committee on Industrial Health of the Massachusetts Committee on Public Safety, those in the second are members of the staff of the Division of Occupational Hygiene, Massachusetts Department of Labor and Industries

INSTRUCTION IN THE DIAGNOSIS AND TREATMENT OF GAS CASUALTIES

Four of the scheduled dates (Springfield, Holyoke, Worcester and Beverly) for the six hour course covering the diagnosis and treatment of gas casualties, published in last week's issue of the *Journal*, were in error. The correct dates are as follows

Springfield	December 15
Holyoke	December 18
Worcester	December 17
Beverly	Undecided

MISCELLANY

VENEREAL-DISEASE CONTROL AND THE PHARMACIST

The United States Public Health Service has recently issued a statement clarifying the role of the pharmacist from the public health viewpoint in the control of venereal disease and emphasizing his importance in the community as an educator, a personal influence and a citizen. Excerpts from the release are as follows

The Pharmacist as an Educator

The pharmacist is an important influence in preventing the spread of venereal diseases, because persons who have these infections frequently go to him for advice or medicine. The pharmacist can make clear to the public that venereal diseases are dangerous, and that to act on the assumption that they are a trifling matter is more dangerous still. He can call on the state or local health department or the state pharmaceutical association for a supply of easy-to-read literature—attractive folders, leaflets, pamphlets and so forth—for free distribution to customers. He can avail himself of colorfully and effectively designed posters from his

tate or local health department for display in his window or elsewhere in the drugstore. He can secure the ready advice and co-operation of such agencies as the Joint Committee of the American Pharmaceutical Association and the American Social Hygiene Association, the National Association of Retail Druggists and the United States Public Health Service. Education is a vital arm in the prevention and control of venereal diseases. The pharmacist is excellently placed to serve an educational role in the community.

The Pharmacist as a Personal Influence

The man who has (or thinks he has) a venereal disease and consults his pharmacist rather than a physician is usually laboring under the misconception that the disease is not serious enough to warrant a physician's attention, or that he can obtain just as effective treatment more cheaply by using a proprietary (patent) preparation sold without a prescription. In either case, he is asking the pharmacist, 'What should I do about my ailment?'

In such a situation, the very presence of a venereal disease victim in a drugstore is fair testimony of the customer's strong personal confidence in the pharmacist. The pharmacist can easily enhance this confidence and add to his good will by exerting his personal influence to guide the customer on the proper course. He can point out the serious character of venereal diseases and the necessity of protecting the individual and the community. He can explain that it is always dangerous to treat oneself with a so-called 'remedy' or nostrum and to assume that one has been cured of syphilis or gonorrhea. He can refer customers who ask for such products to a reputable physician or to a clinic which provides diagnosis and treatment for venereal diseases. He can emphasize that the customer may have a different disease, requiring different treatment from the one he thinks he has, or that he may not even have any disease that a physician is trained to diagnose those diseases with the aid of physical examination and technical laboratory tests. The pharmacist who knows the dangers of venereal diseases and yet continues to diagnose them or to recommend or sell remedies for self treatment does more than violate a fundamental ethic of his profession. He becomes a contributor to whatever disastrous results may follow improper treatment or neglect.

The Pharmacist as a Citizen

As a citizen it behooves the pharmacist to help further the venereal disease control effort in his community by urging and supporting state and local legislation designed to lower the incidence of syphilis and gonorrhea. In some states, the pharmacist can enlist in the legislative campaigns sponsored by his own pharmaceutical organization, by the American Social Hygiene Association and by other health and civic groups, in promoting the enactment of premarital and prenatal laws for blood tests for syphilis. He should familiarize himself with all these activities. He can support legislation opposing advertising of fake cures by quack doctors, and prohibiting the sale of remedies for venereal diseases except by a physician's prescription. He can join the front line forces that are fighting for stricter laws and repressive measures against prostitution. As a citizen, he can insist on adequate treatment facilities for venereal-disease control in his community.

NOTE

The appointment of Dr. A. LeRoy Johnson, of New York City, as professor of clinical dentistry in the new Harvard School of Dental Medicine was recently announced.

gross misconduct in the practice of his profession as shown by his conviction in court.

H. QUIMBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

CORRESPONDENCE

AN OBJECTOR

To the Editor: About 5000 physicians of this state recently received a follow-up letter from the Massachusetts Medical Service (Blue Shield) urging them to sign up as members. These men had, of course, ignored the first invitation to join. They are told that 2300 of 7600 doctors in the state have signed. The letter ends as follows: "Sign today for a free profession charting its course in a revolutionary world. Will your boy be a free practitioner in America's tomorrow? Here are the agreements. There is the pen. Please sign."

Of all the high-power and pressure advertising over the radio designed to sell hair tonic or stock in a gold mine, none is more ridiculous or insulting to men of intelligence than this. This whole scheme has been put over on the 7000 men by the 600 who have an ax to grind. And then we are told that it is a plan worked out by the Society for the general good. Who is the Society? How many signed statements can they get from members that they were ever consulted or even approved of this plan? I have made it my business to question a cross section of the men at three hospitals with which I am connected and find none who approve. Even those who have signed state that they did so because they felt that they would be frozen out if they refused to do so. If this was a sincere plan for the betterment of all the doctors as well as the public, and not for just a few specialists who occupy the drivers' seats, some provision would have been made for payment of services to the general man. Why just the surgeon, with a sop to the obstetrician? I feel that advantage is being taken of the fact that hundreds of the younger and more active men are in the service, to force this scheme upon us.

May I strongly urge that all of you men who do not approve of this setup as at present planned, refrain from signing. Drop a line to the Massachusetts Medical Service and to the Society and tell them why. We all know that if the time ever comes that state medicine is to be forced upon us, that a plan such as this will not abort it. But in the meantime the specialist will be cashing in. They only have 2300 out of a possible 7600 members, and a great many of these will withdraw if given the opportunity. It is not too late. Fight back NOW!

C. EDWARD GREENE, M.D.

254 Washington Avenue
Chelsea, Massachusetts

* * *

Apropos of Dr. Greene's questions and musings, one cannot help but wonder if he has read the published reports of the meetings of the Council during the past two years and, if so, why he has remained silent so long. En.

DEPRIVATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held November 20, the Board voted to revoke the license of Dr. William P. Grovestein, Scituate, to practice medicine in this Commonwealth because of

BOOK REVIEWS

Lane Medical Lectures: The lymphatic system; its part in regulating composition and volume of tissue fluid. By Cecil K. Drinker, Sc.D., M.D. Stanford University Publications, University Series. Medical Sciences, Vol. IV, Number 2. 4°, cloth, 101 pp., with 29 illustrations. Stanford University, California: Stanford University Press, 1942. \$2.25 (\$1.50 paper).

In a readable and scholarly manner the author gives an authoritative account of the reasons "why mammals have lymphatics; why the lymphatic system has been slowly turned from a casually organized accessory of the blood circulation into a physiological entity, complementing this first system and joining with it in the task of keeping the composition and volume of the mammalian tissue fluid at a steady normal level."

In the opening chapter the author traces the evolution of the mammalian circulation in invertebrates and vertebrates and emphasizes the part that microchemical methods and micromanipulative and macromanipulative dissections play in answering the question why the lymphatic system appears and operates as it does. In keen literary style the author writes: "I have no objection to theories, but they are the cocktails not the roast beef of science." The next three chapters are concerned with the establishment of the capillary circulation, the appearance and elaboration of lymphatic vessels and the experimental evidence drawn from the heart and lungs to show the interdependence of the blood, tissue fluid and lymph. The final chapter deals with the role of the lymphatic system in wounds and in diffuse fibrosis of the lungs following the persistent inhalation of dust.

The book is well illustrated, with historical plates and figures, and an interesting bibliography is appended. Containing outstanding, up-to-date lectures, it should be in the personal library of all scientific investigators.

Anoxia: Its effect on the body. By Edward J. van Liere, M.D., Ph.D. 8°, cloth, 269 pp., with 17 illustrations and 15 tables. Chicago: The University of Chicago Press, 1942. \$3.00.

In clear language the author takes up systematically and in detail the effect of anoxia on all the known physiologic processes of the body. Experimental facts and data are brought together to show the changes wrought by anoxia on the blood, on the heart and circulation and on the blood pressure and lymph and its effects on respiration, on the alimentary tract, on the endocrine glands and on urinary secretion. There are other chapters dealing with investigations concerning the influence of anoxia on metabolism, heat regulation, nutrition, water distribution and the nervous system. To achieve this task in a small book is something for which the author is to be congratulated. There are useful bibliographies at the end of the author's discussion of each system.

For those interested in aviation medicine and in air travel this book will make a strong appeal.

(Notices on page x)

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SKIN DISTURBANCES IN DIABETES MELLITUS: THEIR RELATION TO VITAMIN DEFICIENCIES*

ABRAHAM RUDY, MD,[†] AND RICHARD HOFFMANN, MD[‡]

BOSTON

SKIN disturbances in diabetes mellitus are very frequent. Commonest among them is pruritus, both general and local. The latter is especially observed around the genitalia, in fact, pruritus vulvae is frequent enough to be considered one of the cardinal symptoms of diabetes. Dermatitis is seen in the genital regions, in the intertriginous areas (submammary, inguinal and intergluteal) and in other parts of the body that are exposed to irritation of any kind. Fissures in the corners of the mouth and in the temporal angles of the eyes and changes in the nails and hair are frequently observed if carefully watched for. The skin in diabetic patients seems to be predisposed to pyogenic and mycotic infections. One thus finds, not infrequently, furuncles, carbuncles, pyoderma, hydrous adenitis axillaris, ecthyma and mycotic, especially monilia, infections of the skin. The frequency of these conditions in diabetes has prompted dermatologists to look for a disturbance in the carbohydrate metabolism whenever they are found. The literature is full of reports of this kind. Many of these patients have been subjected to glucose tolerance tests to discover a latent disturbance in the carbohydrate metabolism. In cases with normal glucose tolerance tests, skin sugar tests have been carried out.

There is a natural tendency to relate the sugar in the urine or blood or the various substances of the intermediary carbohydrate metabolism to most of the complications of diabetes. The increased blood sugar, as well as the sugar in the bodily excretions, such as sweat, saliva and urine, and in the skin itself, has been considered as a possible cause of the skin disturbances.

About five years ago one of us (A. R.) began a study of the various manifestations of vitamin deficiencies and their frequency in diabetes mellitus. It was soon found that skin lesions were not uncommon among our patients with such deficiencies. To evaluate the skin disturbances more carefully a dermatologist was assigned to the Diabetic Clinic of the Beth Israel Hospital. Our observations to date are that the skin manifestations in diabetes mellitus are frequently of the pellagrous type and that, on careful observation, signs of a deficiency of one or more components of the vitamin B complex, either before, during or after the discovery of the skin disease, can be revealed. At times there are also manifestations of a deficiency in other vitamins.

The following cases are presented to demonstrate that the skin disturbances in diabetes mellitus are most frequently due to a vitamin deficiency, especially that of nicotinic acid.

CASE REPORTS

CASE 1. A. K. (B. I. H. No. 1137A), a 41 year old woman, was discovered to have diabetes in 1934. She was usually careless with her diet, and took 70 units of insulin daily. In November, 1939, she developed skin lesions under the breasts and in the axillae. The skin of the submammary regions showed sharply defined, isolated and coalescent round and oval, slightly raised lesions, partly scaly, dry and red, from 5 to 30 mm in diameter, the axillary skin was red, dry, slightly indurated and partly peeling, the surrounding areas showed small, isolated, scaling lesions (Fig. 1). The urine showed sugar and the blood sugar was elevated.

The patient was started on 150 mg. nicotinic acid orally daily. After 2 weeks her skin condition showed a marked improvement. The nicotinic acid was then raised to 300 mg. daily. After 2 weeks the skin showed only pigmentation at the site of the subsiding lesions. By January, 1940, the skin was completely clear (Fig. 1) in spite of the fact that the diabetic condition remained uncontrolled. No local treatment was applied all this time. The nicotinic acid was then discontinued.

*From the Medical Service and Skin Service, Beth Israel Hospital. Aided by a grant from the Charlton Research Fund, Tufts College Medical School.

The vitamin used in these studies were kindly supplied by Merck and Company, Incorporated, Rahway, New Jersey.

[†]Instructor in medicine, Tufts College Medical School, associate visiting physician at the Diabetic Clinic, Beth Israel Hospital.

[‡]Junior physician, dermatologist at Beth Israel Hospital.

In February, 1941, the patient developed a severe pruritus vulvae with a vulvitis greatly disturbing her sleep. Her diabetes was still in the same poorly controlled condition. Because of a vaginal discharge she was referred to the Gynecological Clinic, where no explanation for the

and the pruritus vulvae cleared up in spite of the fact that the diabetes remained uncontrolled.

CASE 2. F. G. (B. I. H. No. 3593A), a 61-year-old woman, was found to have diabetes in 1929. She was on a diet



FIGURE 1. Case 1.

Skin under breasts before (left) and after (right) the administration of nicotinic acid.

pruritus vulvae was found. She was given vaginal douches and local treatment without relief. The pruritus vulvae gradually grew worse, and in June she developed for the second time lesions under the breasts similar to those found in 1939. The pruritus vulvae was still very severe

until 1932, when she was started on insulin. Pruritus vulvae developed in 1933 and cleared up without any special treatment. In June, 1938, she again developed pruritus vulvae, which disappeared after the insulin dosage was increased. The following August she presented an

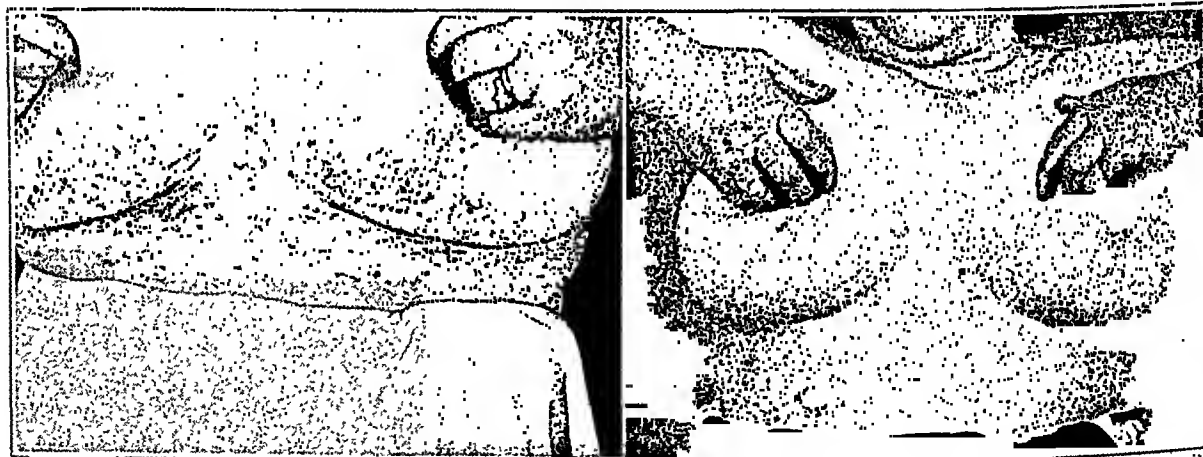


FIGURE 2. Case 1.

Skin under breasts on recurrence (left) and subsequent disappearance (right) following the administration of nicotinamide.

and distressing. The patient was started on nicotinamide and received from 250 to 450 mg. orally daily and eighteen injections of 100-mg. doses parenterally in about 2 months. This resulted in an almost complete disappearance of the submammary skin lesions and of the vulvitis (Fig. 2).

Comment. In this case the skin lesions and the vulvitis represented manifestations of pellagra. They responded to nicotinic acid treatment and returned with its omission. Large doses and parenteral administration of nicotinamide were then necessary. It is worth noting that the skin

erosio interdigitalis on her right hand for about a week. In 1939 she developed a severe pruritus vulvae and an (Fig. 3) and other skin lesions. The skin in the groins and in the perianal region was deeply red and shiny in a sharply defined area. In the inguinal folds there were deep, bleeding fissures, while the skin of the labia minora and the mucous membrane of the vulva were red, slightly edematous and showed a whitish loosely adherent, spotty membrane. Under both breasts there were small, isolated, sharply defined reddish lesions somewhat elevated and slightly peeling. The skin of both cubital

regions, the inner side of the thighs and the lower part of the abdomen showed erythematopapulous eruptions.

corners of the mouth (perlèche) for a short time. In December, 1941, she complained of a severe dermatitis

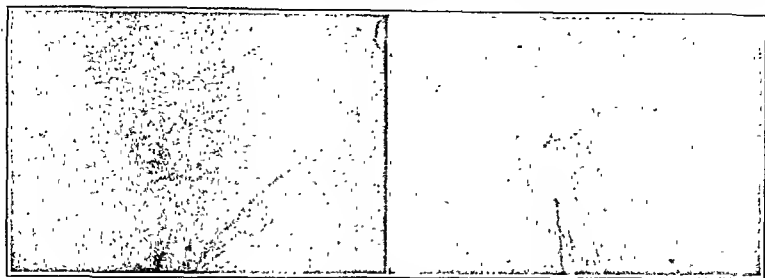


FIGURE 3. Case 2.

The anal region before (left) and after (right) the administration of nicotinic acid.

Cultures from these areas revealed *Monilia albicans*. The skin condition did not respond to local treatment.

In October, 1939, the patient was started on daily doses

in the left ear canal. The skin of the meatus auditorius was red, dry, scaly and indurated. She was given nicotinic acid up to 300 mg. daily for several weeks without

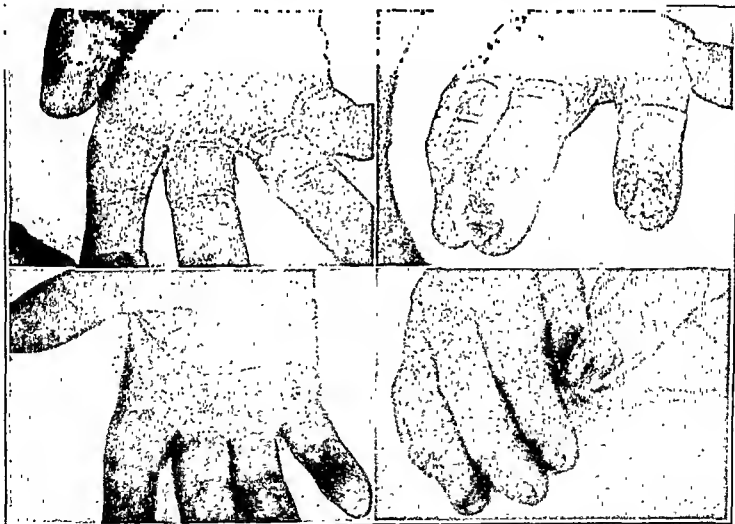


FIGURE 4. Case 3.

The palmar skin and nails before (upper) and after (lower) the administration of nicotinic acid and vitamin B complex.

of 150 mg. of nicotinic acid orally. This was continued until February, 1940, when the pruritus vulvae and ani completely disappeared in spite of the fact that the diabetic condition remained unchanged (Fig. 3). In March the pruritus vulvae recurred and cleared again with nicotinic acid. In 1941 the patient showed fissures in the

local treatment and the dermatitis in the ear completely cleared up.

Comment. The interdigital, vulvar, anal and ear lesions in this case represented pellagra. They responded to the treatment with nicotinic acid. Here again the skin improved, although the diabetes remained unchanged. This

case illustrates that the skin lesions do not always occur simultaneously and therefore are frequently incorrectly diagnosed.

CASE 3. M. F. (B. I. H. No. 57214A), a 70-year-old woman, was seen for the first time in July, 1939, when she was admitted to the wards because of a generalized

trol of the diabetes by diet and very small doses of insulin, and with the administration of vitamin B complex, vitamin B₁ parenterally and nicotinic acid orally, 300 mg daily, the skin condition was much improved in a very short time (Fig. 4). No local treatment was used. The mental and general condition also improved. The vivid red in the genital and perianal regions changed to a

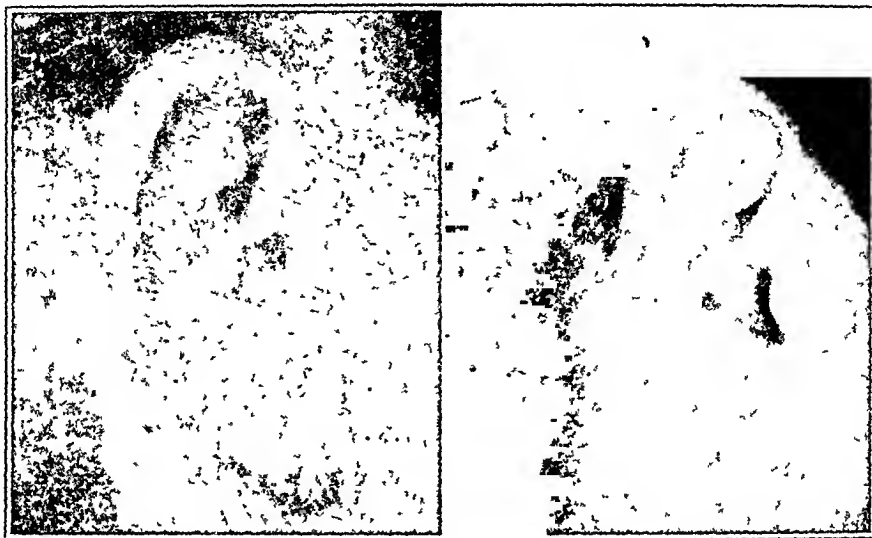


FIGURE 5. Case 4.

The auricle before (left) and after (right) treatment with nicotinic acid.

dermatitis. Diabetes mellitus was discovered on admission. There had been a loss of weight for about 2 years. On examination the tongue was beefy. The skin of both palms was dry, macerated, thickened, scaly and cracked. The interdigital folds were macerated and fissured. The skin of the dorsum of the hands was rough, red, dry, indurated and slightly peeling. The skin on both knees and elbows was dry, rough and red. The fingernails consisted of soft lamellar masses (Fig. 4). The skin

reddish, dark-brown discoloration, which gradually subsided.

A few months later the patient developed an acute psychosis with amnesia for certain happenings and hallucinations. She became violent and was admitted to a hospital for chronic patients. In spite of large doses (1000 mg. daily) of nicotinic acid, she succumbed in a psychotic state.

Comment. This patient presented a classic picture of acute diabetes mellitus with pellagra. The skin manifestations responded well to treatment with nicotinic acid, while the psychosis did not.

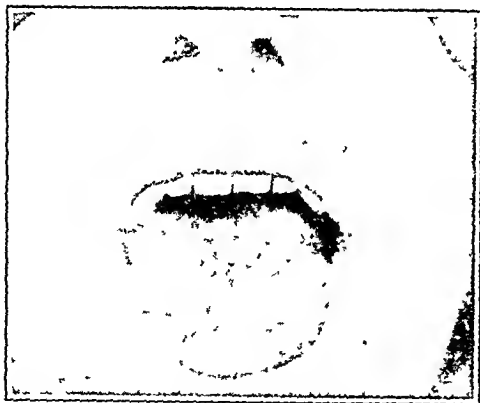


FIGURE 6. Case 5.

This photograph shows the smooth tongue.

of the genital, inguinal and perianal regions was dry, indurated, red and rough.

The neurologic examination showed absent abdominal reflexes and knee and ankle jerks. The arm reflexes were present. There was a positive Hoffmann's sign on the right and a grasp reflex. The mental picture was somewhat similar to Korsakoff's psychosis. With the con-

CASE 4. R. N. (B. I. H. No. 33806A), a 46-year-old woman, was found to have diabetes mellitus in 1934, with an acute pruritus vulvae, which cleared up with the control of the diabetes. She was not seen for 4 years. On her return to the clinic in November, 1939, she admitted being careless with her diet. She complained of an itching skin eruption on the ears, under the breasts and in the pubic and sacral regions of 3 years' duration. The skin of both ears was indurated, red, dry and partly covered with slightly adherent whitish scales (Fig. 5). The retroauricular and intra-auricular regions showed similar skin changes in sharply defined areas with oozing, partly crusty, deep fissures. The skin under the breasts showed slightly scaly, isolated lesions on a somewhat indurated and slightly erythematous base. A few similar lesions were found in the pubic, intergluteal and sacral regions. The skin in the regions of the olecranon and the patellas was rough, somewhat scaly and indurated. The lips were dry. There were fissures with some induration in the corners of the mouth.

The patient was given a diet and insulin. In addition, lanolin was applied locally. In 1 month the diabetes was under control. The skin of the ears was paler, still dry

and indurated, with a few scales. The retroauricular region still showed induration, scaliness and fissures. The skin under the breasts and in the pubic and sacral regions showed no improvement. The patient was started on 200 mg of nicotinic acid orally daily, without any local treatment. The diet and insulin dosage remained un-

changed. The diet and insulin dosage remained unchanged. The diet and insulin dosage remained un-

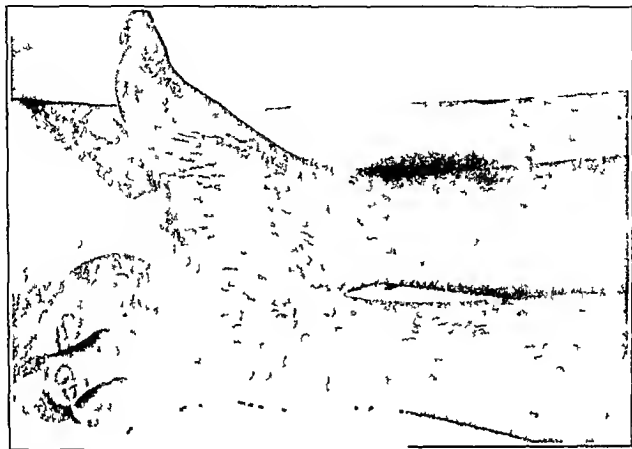


FIGURE 7 Case 5

Feet and lower legs showing dry shiny atrophic skin

changed. Within 2 weeks all the skin manifestations including the fissures in the corners of the mouth, showed improvement. Two weeks later the skin almost completely cleared up. The patient was continued on 150 mg nicotinic acid orally daily for 2 more weeks. The skin remained clear (Fig 5). This time, however, she returned with symptoms of a peripheral neuritis, namely, pain and numbness in the hands and fingers and a tingling sensation in both legs. The nicotinic acid was omitted, and she was started on yeast tablets.

Comment. This patient showed the skin manifestations of an atypical pellagra. She presented symptoms of a deficiency of the various components of the vitamin B complex. It is possible that the neuritis was precipitated by the intensive nicotinic acid treatment without the use of the entire vitamin B complex. It is generally believed that the administration of large doses of one vitamin increases the demand for the other vitamins.

Case 5. B F (B I H No 48848), a 39-year-old woman, was admitted to the surgical wards because of a carbuncle on the back. She gave a history of diabetes mellitus of 6 years duration, controlled by diet and insulin. The urine was sugar free most of the time. She was irregular with her meals, and frequently omitted her lunches. For at least 4 years she had complained of attacks of pruritus vulvae, dysuria and generalized pruritus, in spite of the absence of sugar pus or bacteria in the urine.

The patient stated that her skin had been very shiny and paperlike for about 2 years. On examination she

showed a beefy tongue, perleche and a dry, shiny and somewhat atrophic skin with areas of depigmentation and hyperpigmentation. The skin on the back showed a carbuncle and numerous superficial ulcerations, surrounded by indurated brownish red dry and scaly areas. There was also a marked vulvitis. The blood pressure was

140/80. The urine was sugar free with large traces of albumin. The carbuncle was incised. In addition to the diet and insulin, the patient was given vitamin B complex and 300 mg of nicotinic acid orally daily and also vitamin B₁ intramuscularly. She was discharged improved 9 days after admission.

In August, 1940, the patient returned to the medical wards. She had developed a severe hypertension in the meantime and 2 weeks before the second admission began to have severe attacks of vomiting and dizziness. Because of the vomiting she had limited her diet and eaten very little. She continued, however, to take her insulin. On examination she showed a blood pressure of 260/130. The fundi showed marked edema of the disks, with old and fresh hemorrhages and cottonlike exudates. The heart was enlarged to the left. There were numerous rales at the right base, with dullness to flatness. The tongue was red and smooth (Fig 6). The skin showed a marked progression in the changes described on her previous admission (Fig 7).

Laboratory data revealed no anemia, total protein 4.5 gm per 100 cc, nonprotein nitrogen 35 mg per 100 cc, circulation time 30 seconds, basal metabolic rate -4 per cent, spinal fluid protein 51 mg per 100 cc, and a negative gastrointestinal series. The urine showed large traces of albumin.

In addition to the multiple vitamin deficiency state a diagnosis of intercapillary glomerulosclerosis was made. After discharge the patient developed generalized edema and received mercurial diuretics regularly from her family physician. In November, 1940, she was readmitted in a

comatose state. Her condition grew rapidly worse, the temperature rose to 104°F., and she expired on the 6th hospital day.

Comment. This case showed definite signs of pellagra, such as the beefy tongue, perleche and vulvitis. Whether the skin changes were due to the vitamin B deficiency alone or also to a vitamin A deficiency, we are still unprepared to say. In this case also the pruritus vulvae was present for many years in the absence of glycosuria.

DISCUSSION

In addition to the cases described above we have seen many more diabetic patients with similar more or less pronounced skin eruptions. A review of the literature to date shows that the entire subject is unsettled and somewhat confused. There is still a widespread belief that the skin lesions in diabetes mellitus are in some way related to the disturbed carbohydrate metabolism, although Goldsmith¹ and Rost² definitely expressed their doubt that certain groups of skin diseases are regularly connected with hyperglycemia. In 1931, Rudy³ discussed the relation of the skin to the carbohydrate metabolism and reviewed the literature. At that time very little was known about the skin manifestations. In addition to the glycosuria and hyperglycemia, the increased sugar in the sweat⁴ and in the skin^{5,6} were considered as possible precipitating causes of the skin lesions. Hesseltine,⁷ who made a special study of vulvovaginitis in diabetic patients, claims that "synthetic glycosuria" does not produce vulvitis or pruritus. He believes, however, that glycosuria provides a good medium for fungus infections. Goldsmith¹ states that the diabetic skin is more easily infected with monilia than normal skin, but admits that the severity of the infection does not coincide with the degrees of hyperglycemia. Greenwood and Rockwood⁸ believe that in diabetic patients the monilia infections affect the mucous membrane of the vulva and may extend to the skin, whereas in nondiabetics it is commoner in the groins and axillas and under the breasts. Greenwood⁹ divides pruritus ani in diabetic patients into three types: Type 1 shows a definite infection of the skin with bacteria; Type 2 shows an infection with fungi; and Type 3 has no change in the skin. His treatment varies but is local. Lamb and Keltz¹⁰ in 1941, in a paper on skin manifestations in diabetes mellitus, state that the decreased resistance of the uncontrolled diabetic patient to infections of the skin is still unexplained but that it is definitely related to the control of the diabetes. In 1940 Rudy¹¹ stated that skin manifestations of the pellagrous type are not uncommon in diabetes mellitus.

The skin of some of the diabetic patients is not unlike that of the pellagrins. It shows an increased vulnerability to any kind of external irritation (rubbing or other mechanical or chemical trauma,

perspiration, heat or sunlight) and to infections, especially those due to monilia. We have shown in our cases that vulvitis as well as pruritus vulvae and ani in diabetes are proved signs of pellagra and are due to a nicotinic acid deficiency. It is interesting that in 1908 Nicholas and Massia¹² gave a description of pellagrous vulvitis and perivulvitis that coincides exactly with our observations in diabetic patients.

As a result of old textbook descriptions of the skin lesions in pellagra, there is still a tendency to relate the diagnosis of pellagra with the classic picture in which the face, the neck (*collier de Casal*) and the back of the hands are pointed out as the typical localization, as opposed to atypical localization in other parts of the body.

Exposure to sunlight was considered as one of the main etiologic factors of the pellagrous skin manifestations. Today it is known that exposure to sunlight is only one of the irritants and not at all one of the most frequent.

In the same way we cannot always expect to find the fully developed picture of pellagra, consisting of dermatitis, glossitis, gastrointestinal disturbances and mental changes. The skin lesions, like some of the other manifestations, may be missing or may be so mild and in such a localization that they can be completely overlooked. Since dermatitis was formerly the most important diagnostic finding in pellagra, in its absence cases were diagnosed "pellagra sine pellagra." The localization of the skin lesions in pellagra depends on the site of the exposure to irritation of any kind. One may find skin eruptions in any part of the body in lesser or in greater degrees, and they should be looked for in areas that are exposed to irritation. Wherever a single lesion suggesting pellagra is observed, a careful examination frequently reveals other skin lesions or some other signs of pellagra, such as glossitis, pruritus vulvae or gastrointestinal or mental disturbances.

Most of the manifestations of pellagra respond to treatment with nicotinic acid. Since nicotinic acid is a component of the vitamin B complex, a careful search often discloses that signs of a deficiency in the other components, such as riboflavin and thiamine chloride, have preceded or are present, or such lesions may be expected to follow.

The morphology of the skin lesions depends on their localization, the thickness of the involved horny layer, the quantity and quality of the local irritation and the severity and duration of the deficiency. The most frequent manifestation is a vivid, more or less indurated erythema, which is characterized by a violaceous or brownish color and a definite shine on the surface. Fine lamellar peeling or psoriasiform scaliness, more or less deep ridging of the papillary lines and fissuring, edema,

Loss of weight, infections, gastrointestinal disturbances, acidosis, overindulgence in alcohol and operations may act as precipitating factors in the development of the deficiency symptoms in diabetes mellitus.

CONCLUSIONS

Skin disturbances are common in diabetes mellitus.

They are not related to the glycosuria or hyperglycemia but are due to an increased vulnerability of the skin as a result of a deficiency in the components of the vitamin B complex, especially nicotinic acid.

Furuncles, carbuncles and other pyogenous as well as mycotic infections may occur alone or combined as a result of this vulnerability.

Pellagrous dermatitis in diabetes is especially frequent and is often diagnosed and treated as psoriasis vulgaris.

Pruritus vulvae and ani in diabetes are a manifestation of pellagra and respond to treatment with nicotinic acid.

A careful history and physical examination in these cases will invariably disclose manifestations or signs of a multiple vitamin deficiency, a beefy or smooth tongue, cheilosis and gastrointestinal, genitourinary, neurological, mental and other disturbances. These signs in the various systems of the body do not always occur simultaneously. They may precede or follow the skin disturbances.

The skin lesions may improve, remain unchanged or even become aggravated with the control of the diabetes by diet, with or without insulin. They always respond to treatment with nicotinic acid. The monilia infections clear up without local treatment. A complete cure from nicotinic acid treatment may take from a few days to several months. The more stubborn cases require fairly large doses parenterally as well as orally.

Since the vitamin deficiency is frequently multiple the entire vitamin B complex should be administered in addition to the nicotinic acid, which can also be given in the form of nicotinamide.

Recurrences are not uncommon if the underlying cause is not or cannot be removed. Infections, gastrointestinal disturbances and acute upsets in the carbohydrate metabolism predispose to recurrences. The administration of vitamin B complex may therefore become a permanent necessity for some patients.

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MESENTERIC THROMBOSIS IN MENTALLY ILL PATIENTS*

CONRAD BELL, M.D.,† WILLIAM CORWIN, M.D.,‡ O CAR J MARCIL, M.D.,§
AND ELVIN V. SEMRAD, M.D.¶

WALTHAM, MASSACHUSETTS

THE diagnosis of occlusion of the mesenteric circulation by venous thrombosis or embolism is often difficult and is usually made at operation or autopsy. The problem becomes somewhat more difficult when a patient suffering a mental illness, handicapped in his communicability, suffers a mesenteric thrombosis or embolism. We have had opportunity to study 5 cases in the last five years, 2 verified by autopsy, 1 by operation and 2 by clinical methods. Of the latter, one patient died and we were unable to perform an autopsy, and the other recovered without operation. As the last 2 cases mentioned are open to considerable question because of lack of verification, we shall emphasize the 3 cases that we had a chance to verify.

Pollak,¹ emphasized the importance of this disorder because of the severity of its effects rather than because of its frequency; he stated that the literature up to 1937 contained reports of about 500 cases, many of which were collected by Galvin.²

There are certain points that suggest the diagnosis. Although the disease may occur at any age, even in childhood,⁴ it is more commonly a disease of later life. It is usually associated with some disease of the circulatory system, such as endocarditis, atheroma of the aorta or arteriosclerosis, and there may be a history of embolic phenomena in other parts of the body before the onset of abdominal symptoms, or simultaneously with them. It has occurred in patients with chronic diabetes.

The classic signs and symptoms are severe abdominal pain (generalized over the abdomen, constant or in exacerbations), vomiting, melena and distention of the abdomen with tympanites and at times a shifting dullness in the flanks. Blood was present in 41 per cent of the cases reported by Jackson et al.⁵ When the process of infarction involves the upper intestines, a vomiting of blood has been reported. The patient may show signs of collapse, with a fall in body temperature. A low pulse rate is sometimes found at the onset of the attack. The leukocyte count is elevated, in the series of 92 cases collected by Meyer⁶ the

count in all but 3 averaged 18,000, the highest being 45,000. Dunphy and Zollinger⁷ stressed the fact that although the clinical picture varied considerably, several important features could be recognized in such cases. First, it was observed that regardless of the duration of the attack, the clinical picture was not typical of any of the common surgical emergencies. The localized tenderness of appendicitis, the rigidity of perforated ulcer, the visible peristalsis and early distention of acute intestinal obstruction were not present. It was not the problem of a mistaken diagnosis but of no diagnosis. However, the patients were obviously ill from an abdominal lesion that simulated obstruction. Secondly, the character of the pain in each case was out of proportion to the clinical picture. This was so striking in one case that the staff favored a diagnosis of hysteria. Another significant characteristic of the pain was its persistence after the usual measures for its relief such as, small doses of morphine, enemas and continuous gastric lavage, had been instituted. Thirdly, the only constant physical finding was abdominal tenderness, more or less generalized, with rebound tenderness referred to the point of pressure. Fourthly, all the patients had a relatively high leukocytosis, a high or mounting pulse rate and a temperature that was normal or only slightly elevated. Finally, it was evident in each case that there was a gastrointestinal disturbance, but this was not manifested in any constant manner. Difficulty in moving the bowels without evidence of complete obstruction was seen in all cases. Vomiting was variable and bloody diarrhea did not occur. Rapidly progressing shock was seen in 1 case.

McIver⁸ in a series of 9 cases found 3 in which the circulation was occluded in other ways than by mesenteric thrombosis.

Clinical manifestations are quite varied. Many cases cause no symptoms suggesting mesenteric thrombosis and the condition is found only at autopsy.⁶ Some run a chronic and some an acute course.⁵ In the larger, acute group there may be a sudden onset of colicky pain characteristic of obstruction, often at a time when the patient is in good health. Death usually follows in a few days or even hours. The pain is usually generalized over the abdomen; it may be constant and extremely severe, although not infrequently there

*From the Metropolitan State Hospital, Waltham, Massachusetts.
†Consulting surgeon to Waltham Hospital, Metropolitan State Hospital and Walter E. Fernald State School.

‡Assistant superintendent, Metropolitan State Hospital, instructor in psychiatry, Boston University School of Medicine.

§Formerly senior physician, Metropolitan State Hospital, staff member, Gardner Hospital, Gardner, Massachusetts.

¶Senior physician, Metropolitan State Hospital, instructor in psychiatry, Boston University School of Medicine, assistant instructor in psychiatry, Harvard Medical School.

are exacerbations with comparative comfort between attacks.

Brown⁹ stated that 772 cases of both arterial and venous occlusion had been reported in the literature. He studied 104 cases of venous mesenteric occlusion. Other reports were reviewed¹⁰⁻²¹ to compare the problem as it exists in patients in general hospitals with that of those suffering from mental illness.

The group of cases that run a chronic course is smaller; onset is insidious, and they may go on to a spontaneous cure. Cases in the literature²²⁻²⁹ have been reviewed in comparison with our own.

In our cases a differential diagnosis not usually mentioned in the literature arose, that is, the evaluation of the problem of head injury or intracranial disease. One of Abrams's³³ cases is suggestive of possible intracranial complications, which were not verified at autopsy. This patient (Case F), aged thirty-two, suffered rheumatic heart disease with fibrillation, and two weeks before the discovery of mesenteric thrombosis was seized suddenly with a severe pain on the left side of the head, after exertion caused by moving heavy objects. It lasted five days and was diagnosed as an embolus in a silent area of the brain, in the absence of neurologic findings. Feeling better for a time, the patient got up to go to the bathroom, and while at stool was suddenly seized with a violent attack of pain in the midabdomen, which at autopsy was proved to have been due to mesenteric thrombosis.

CASE REPORTS

CASE 1. J. F. D., a 58-year-old fireman, was diagnosed as having psychosis associated with organic changes of the nervous system and paralysis agitans.

The paternal grandmother was said to have had mental symptoms following the menopause. The maternal grandfather died of diabetes.

Little was known about the patient's childhood diseases. A sister believed that he had typhoid fever when he was 8 years of age. She stated that in 1932 or 1933 he suffered from two "shocks" but continued working for nearly a year following them. In 1933 he began to have difficulty with his eyesight and was gradually relieved of most of his duties because of physical disability. At this time he walked in a stooped manner, with the arms held in an "ape-like," semiflexed manner. His memory began to fail, and he made mistakes in his work. Neurologic examination in October, 1933, yielded the diagnosis of paralysis agitans, probably on an arteriosclerotic basis. About this time he began to show more prominent mental symptoms, becoming restless, emotionally unstable, confused and incontinent. He was admitted to the hospital in July, 1935.

In the evening of November 6, 1937, the patient vomited a small amount of undigested food about 1 hour after supper. He slept all night. At 7:35 the next morning he fell out of bed, but was not unconscious. Contusions of the left eye and of the right frontoparietal region were noted. The temperature, pulse and respirations were nor-

mal. On November 8 the patient vomited twice after supper. The temperature was 99°F., the pulse 98, and the respirations 22. A soapsuds enema was given, with good results. He vomited large amounts of greenish fluid twice during the evening. On the morning of November 9 the patient vomited thick, viscous, brownish coffee-grounds material; the vomiting was described as projectile. The color was poor, the pulse was weak, and the patient seemed to be in a state of semicollapse. The blood pressure was 90/0. He was incontinent. His general condition improved after a stimulant. A spinal-fluid examination showed a pressure of 50 mm. (water), a protein of 70 mg. per 100 cc., a sugar of 120 mg., a chloride of 837 mg. and a red-cell count of 1000. At 1 o'clock the pulse was very weak and irregular; the patient was incontinent and vomited again a small amount of fluid. There was some twitching of the arms and legs. The respirations were labored and irregular, at times being recorded as low as 4 per minute. The skin was warm. He continued to be nauseated and attempted to vomit. A neurologic examination the evening of the same day was reported as follows:

The patient is pale, emaciated and semicomatose. He resists and groans whenever attempts at examination are made. The pupils are equal, of medium size, and react to light. The eyegrounds show congestion of the retinal vessels. The disks are congested, but the edges are clear. No papilledema is noted. There is no exudate. There is slight weakness in the left lower face. The patient lies on his right side in a jackknife position, with the arms crossed on the abdomen. Attempts to extend the arms and legs meet with severe resistance. The abdomen is rigid and boardlike. Palpation of the abdomen is electively painful. There is no paralysis of voluntary movements in the upper or lower extremities. The tendon reflexes are blocked by voluntary flexion and spasm. The plantar reflexes are flexor bilaterally. The spinal-fluid findings appear to be rather baffling. There are no neurologic signs pointing to intracranial injury, but there is a left-lower facial weakness, which may be related to the history of paralysis agitans of some years' duration. Profuse vomiting of brownish, viscous material, pain and abdominal rigidity, with signs of collapse, make it necessary to eliminate an abdominal condition before considering intracranial injury or cerebral accident.

A surgical consultation was held and it was found that the patient was practically moribund. The recti muscles were very spastic but the sides of the abdomen were comparatively soft. At 9:15 p.m. the patient suddenly grew weaker. Coarse, moist rales were present in both lung fields. The temperature was 101.8°F.; the white-cell count was 17,450. He was pronounced dead at 9:55 p.m.

Autopsy. The stomach appeared enormously dilated. There were numerous bloody retroperitoneal adhesions beginning at the sigmoid, following up the descending colon and extending to the lower edge of the left kidney. Over the sigmoid the color was greenish, indicating beginning gangrene. The transverse and descending portions of the colon were filled with hard masses. The vessels of the mesentery were excessively engorged. The duodenum was quite distended, and there was no constriction therein or at the pylorus. Below the pylorus was a tear in the duodenum about 1.0 cm. in length. The stomach contained about 1000 cc. of greenish fluid, with some heavy, solid food mixed with it. The mucous membrane of the

stomach was moderately injected. The brain showed no evidence of subdural or intracranial hemorrhage. Diagnosis: mesenteric thrombosis, rupture of duodenum, lobar pneumonia.

CASE 2 B F M, a 61 year-old garage mechanic, was diagnosed as having manic depressive, depressed, psychosis.

At the age of 7 the patient had an attack of meningitis, from which he made a good recovery. An appendectomy was performed in 1905, following which he was ill for many months. In 1911 he was in bed for 11 weeks, suffering from a duodenal ulcer, accompanied by severe hemorrhages. In 1920 he had a severe attack of mumps but suffered no serious sequela. Since 1911 he had had periodic attacks of constipation, nausea and vomiting, probably related to his ulcer, although cancer was suspected. An x-ray examination in 1932 showed the stomach to be normal but the first part of the duodenum was continually deformed by a large ulcer. While in another mental hospital between the years 1932 and 1937, —exact date unknown,—he suffered at one time from a severe hemorrhage and was seriously ill. On May 6, 1937, he complained of abdominal pain, which improved following a Sippy regime. X-ray examination of the gastrointestinal tract at this time revealed a deformity of the duodenum believed to be an old ulcer scelerosis.

On January 5, 1938, at 11:45 p.m., the patient attempted to get out of bed, became dizzy, and fell backward, apparently striking his head on the wall. He was unconscious for 5 minutes, during which time the attendant was unable to get the radial pulse. Later, he stated that he felt very weak, confused and dizzy. There was no external evidence of injury to his head. The temperature was 99.4°F, the pulse 114 and of good quality, and the respirations 20. He slept fairly well during the rest of the night, but the next morning he still complained of being somewhat dizzy and appeared weak and somewhat drowsy. The blood pressure was 104/52. He ate his breakfast and noon meal without difficulty. The next morning (January 6), the temperature was 99.4°F (rectal), the pulse 100, and the respirations 20. The patient stated at this time that he had been vomiting off and on for weeks, with pain in the abdomen radiating to the back. At noon the temperature was 100.2°F, the pulse 124, and the respirations 22. A neurologic examination at three o'clock revealed the left knee jerk as slightly more active than the right, and the right ankle jerk as slightly more active than the left. Bilateral Babinski signs were present, with some impairment of position in the toes. The eyegrounds revealed retinal sclerosis. A preliminary diagnosis suggested vascular accident, on the basis of cerebral arteriosclerosis, vascular thrombosis and intra-abdominal bleeding. At 3:15 p.m., the patient complained of severe abdominal pain. He became cold and clammy and moaned and complained of severe pain in the back, and perspired profusely. The right upper quadrant of the abdomen was tender, with spasm. The blood pressure was 58/0, and the pulse 140. The red cell count was 2,860,000, with 49 per cent hemoglobin, and the white-cell count was 9800. Surgical consultation yielded the following note:

Patient in collapse, cyanotic, with poor pulse. Abdominal examination shows a scaphoid abdomen, with no marked spasm. A small tumor mass is felt to the left of the umbilicus, which is not movable. I think this is a case of hemorrhage in the bowel, possibly from the duodenal ulcer. Advise transfusion 250 cc., today, repeat tomorrow.

The patient was able to locate the pain as being centered in the abdomen and also as present over the inferior angle of the right scapula. His condition rapidly became poorer, and he failed to react to stimulants and to intra-venous saline and glucose. He was being prepared for transfusion when he expired, at 6:53 p.m. Shortly before death the respirations became Cheyne-Stokes in nature. He remained conscious until a few minutes before death.

Autopsy The abdominal organs in situ presented a striking appearance in their diffuse, red, wine-like color. The omentum was thin and reddish, with engorgement of the veins. When it was reflected, the transverse colon and sigmoid appeared immensely distended and had the color and appearance of a ripe eggplant. The deep peritoneal cavity contained free, port wine-colored fluid. The surfaces of the visceral and the parietal peritoneum were smooth and glistening. There were no adhesions or exudate anywhere except for a thick, fibrous adhesion of a fringe of omentum to the parietal peritoneum in the right iliac fossa. There was no pus. The congestion of the large intestine was present throughout its distal iliac portion but showed only in spots and patches in the higher segments of the small intestine. The appendix was absent. The stomach had a whitish color and appeared to be distended with a large amount of fluid. The liver was smooth, pale brown and homogeneous in consistence. The gall bladder was distended with liquid contents. The stomach was filled with a large amount of pinkish black liquid and many spongelike lumps, apparently clotted blood. The gastric mucosa was pale and showed no erosions, masses or ulcerations in its wall. The duodenum and the proximal portion of the jejunum were filled with greenish black material. Proceeding distally, there was increasing congestion of the intestinal mucosa, and in the ileum it appeared as if lined with a thick mass resembling currant jelly, red wine in color. In the proximal portion of the ileum the contents of the intestine were frankly bloody. The mucosa was deep purplish red. The cecum was filled with what appeared to be thick, coagulated blood. The contents of the colon was fresh blood. The sigmoid was filled with soft fecal masses, black and homogeneous in color. There was no evidence of intracranial injury. Diagnosis: mesenteric thrombosis, associated with intestinal hemorrhage.

CASE 3 M M, a 59-year-old bartender, was diagnosed as having psychosis with cerebral arteriosclerosis.

The patient was born in Italy and came to this country at the age of 2½. He studied music in his early youth. Later he worked as a bartender, until prohibition. He was temperate in his habits. Commitment to a mental hospital occurred in August, 1930, as a result of irritability, fatigue and emotional instability.

In 1926, it was discovered that the patient had diabetes mellitus, and he was treated by means of a diet. Through out his stay in various hospitals he was under treatment for this condition. This was controlled without difficulty by means of diet and insulin. He also suffered from arteriosclerosis, hypertensive heart disease and chronic nephritis. In 1935 and 1936, he suffered from occasional attacks of dizziness and weakness, at times accompanied by convulsive manifestations. In 1937, it was noted that he had a partial hemiplegia of the left arm and left leg.

On December 25, 1937, about 9:30 p.m., the patient vomited large amounts of food. The temperature was 100.1°F, the pulse 90, and the respirations 20. He did not complain, and examination at that time revealed no acute signs. He slept quite well in long nap and in the

morning the temperature, pulse and respirations were normal. Urine examination revealed a brown reduction, and he was given 20 units of insulin. He ate his breakfast, and about 10 o'clock complained of needing an enema, which was given, with very good results. At 12 o'clock he again vomited a large amount of yellow fluid containing sizable pieces of food. At this time he was moaning and groaning considerably and tossing about, and complained of severe abdominal pain. There were tenderness and spasm in the right and left lower quadrants. Although the patient had previously urinated without difficulty, he stated that if he could only pass his urine he would be relieved. He was catheterized and 150 cc. of urine was obtained. A test at this time showed a yellowish-green reduction. About 1:30 a.m. the patient again vomited large amounts of undigested food. The white-cell count was 18,000, with 88 per cent polymorphonuclears. He seemed relieved of pain following this attack of vomiting and stated that he was more comfortable. Another physical examination revealed persistence of tenderness and spasm in the right lower quadrant. A surgical consultation was held and a diagnosis of acute appendicitis was made.

Operation was performed shortly before 5 o'clock. When the abdomen was opened through a right-rectus incision, a large amount of yellowish, clear, free fluid was expressed. Exploration revealed 60 cm. of the small intestine to be quite bluish in color, with several areas of dark-blue spots. It was noted during exploration that several dark-blue spots were growing progressively larger and that the bowel was becoming more discolored. A large area of venous thrombosis in the mesentery of the small intestine was found. The mesentery bled freely and tore easily. There were large, firm, movable fecal masses in the intestines. The appendix was found to be normal. During the operation the pulse rose to 180, became rapid and irregular, and coramin had to be given. Because of the poor condition of the patient, it was found advisable to terminate the operation without resecting the intestine. The abdomen was closed in layers, with a Penrose drain. His condition remained poor although the pulse improved following the use of stimulants.

On December 27, the patient's condition was found to be very poor. He was moaning, apparently in pain, and quite restless. The temperature was 102.4°F., the pulse 144, and the respirations 16. At times the patient was cyanotic and the blood pressure could not be measured. He continued to vomit frequently. Respiration was at times labored and difficult, and the pulse continued to be irregular. The white-cell count was 13,250, with 81 per cent polymorphonuclears. On December 28, the condition was essentially unchanged. The temperature was elevated; the pulse was rapid, thready and of poor quality. The systolic blood pressure could not be obtained. The color was poor. The skin was cold and clammy, and the patient complained of abdominal cramps. On December 29, he seemed to be more comfortable, although he still continued to moan at intervals. There was no distention. He did not tolerate nourishment very well, vomiting occasionally. On the morning of December 30, the temperature was 101.4°F., the pulse 108, and the respirations 20. He continued to have pain but seemed to be in better physical condition. The pulse was of fairly good quality and the patient seemed to be brighter mentally. A white-cell count on the 29th had been 8950, with 83 per cent polymorphonuclears. On the 30th it was 7850, with 73 per cent polymorphonuclears. The urine showed moderate traces of albumin and sugar, with granular and hyaline casts. During the day of December 31, the tempera-

ture rose to 103.6°F., the pulse to 136, and the respirations to 22. The patient did not complain of severe pain, and the pulse was of fairly good quality, although rapid. On the morning of January 1, the temperature was 103.4°F., the pulse 126, and the respirations 26. The patient appeared to be weaker and seemed to be in more pain. He was not very responsive. The pulse at this time was weak and thready. During the day the temperature continued to rise. At 7 p.m. it was 105.4°F., with a pulse of 144 and respirations of 32. The patient was cold and clammy, was quite weak, and the pulse was rapid and thready. He did not respond and appeared moribund. On the morning of January 2, the temperature was 106.4°F., the pulse 160, and the respirations 44. The patient failed to react to stimulants and rapidly grew weaker, and finally comatose. The respirations were shallow and rapid. The extremities were cyanotic. He continued to vomit and finally expired at 7:35 p.m.

Permission for autopsy was not obtained. Diagnoses: diabetes mellitus; mesenteric thrombosis; peritonitis; cardiac arteriosclerosis.

DISCUSSION

The onset of 2 of our cases was with vomiting that was not associated with symptoms suggesting an acute surgical condition of the abdomen, but in a few hours the symptomatology became that of an acute abdominal emergency. In mental patients, vomiting is frequently associated with constipation and the symptoms disappear after enemas.

Two cases presented the differential problem of possible head injury, and in one case the diagnosis was difficult because of the spinal-fluid studies. In such cases, however, a review of past examinations and reports helps one arrive at a decision concerning the neurologic findings added to the clinical picture that may be indicative of head injury.

Severe abdominal pain was present in each case, not particularly abrupt in onset but severe and generalized. Although the patient in Case 1 did not complain of the pain it was evidently quite severe. The vomiting at first was productive of gastric contents, in one case of several hours' duration and in another becoming coffee-grounds in character as vomiting continued. Distention did not seem to be much of a problem in these cases. Bleeding into the intestine was suggested at least in 2 of the cases. (One of us [C. B.] studied a case in a nonpsychotic patient, which was verified by operation. In this case there was melena during the course of the disease.) Shock symptoms were present in all cases. The number of leukocytes was not higher than that usually associated with abdominal emergencies.

The fact that the clinical picture was not typical of any of the common surgical emergencies is important. The past medical histories yielded some information of associated diseases but were not too helpful in making a diagnosis of mesenteric thrombosis. The fact that the patients became so

extremely sick should have suggested the possibility of mesenteric thrombosis.

SUMMARY

Three cases of proved mesenteric thrombosis occurring in mentally ill patients are presented, with a brief review of the problem of diagnosis.

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MALE STERILITY

WALTER W WILLIAMS, M.D.

SPRINGFIELD, MASSACHUSETTS

THE significance of male sterility is best realized if one considers that about one out of seven marriages are barren, and that in about half these matings the husband is either directly or indirectly responsible for the reproductive failure. The problem of male sterility therefore occupies so important a place in sterility investigations that a lack of adequate consideration must inevitably lead to a greatly reduced validity of diagnosis and consequently to much misdirected or useless treatment of both the female and the male partner.

A vast number of normal appearing and acting spermatozoa are usually required to supply a single cell capable of impregnating an ovum. All male sterility is essentially the result of a diminished availability of normal spermatozoa during the fertile phase of the menstrual cycle. For purposes of discussion, male sterility can conveniently be classified under five headings, according to the degree of availability of normal spermia: faulty delivery of spermatozoa; germ plasma aplasia; germ plasma hypoplasia; germ plasma dysplasia, and asthenospermia.

Faults in Delivery

The recognition of faults in the delivery of spermatozoa constitutes no great problem either in

diagnosis or in the incidence of occurrence. A simple examination of the semen to find out if spermatozoa are present in the seminal fluid and a history that takes into consideration the character of the coital act, together with a physical examination of each partner, should be quite adequate in all cases to clear up this point.

Germ Plasma Aplasia

In germinal aplasia, there is a degeneration or lack of development of the germinal epithelium, so that the patient is entirely incapable of spermatogenesis. Accordingly, no spermatozoa are delivered in the seminal fluid. Testicular biopsy furnishes the only reliable means by which germinal aplasia may be differentiated from the azoospermia of epididymal obstruction, and should be employed in all cases of azoospermia before any type of therapy is attempted. A history and physical examination often provide very inconclusive diagnostic information, since with hypoplasia the testes may not be diminished in size or altered in texture, and in epididymal obstruction a perceptible enlargement or thickening of the epididymis may not be apparent. A history of gonorrheal infection is highly suggestive that the trouble is due to epididymal disease, but furnishes far from conclusive evidence.

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†Genetrist, Springfield, Ill.



FIGURE 1. Normal (upper) and Abnormal (lower) Sperm Populations.

Although there is considerable variability among normal spermatozoa, the size and contour are fairly regular, in contrast with those of abnormal spermatozoa.

a = acrosome; b = nucleus; c = neck; d = body; e = posterior end knob; f = anterior end knob; g = tail; h = cytoplasmic extrusion; i = abnormal nucleus; k = microspERM, with deficient acrosome; n = normal sperm head.

Germ-Plasm Hypoplasia

Germ-plasm hypoplasia signifies an inability of the germinal epithelium to maintain a normal rate of spermatogenesis. The diagnosis is made with the aid of a blood-counting chamber, and the count should be made on a specimen obtained after a period of four or five days' sexual rest. Frequency of intercourse, even in normal persons, may reduce temporarily the number of spermatozoa in a given ejaculate, and accordingly it is well that a low density count should always be rechecked with another sample obtained under known conditions. A moderate hypoplasia with a normal sperm population may be of little clinical significance, and warrants a relatively good prognosis, particularly if the case is handled properly from the medical point of view and a sexual overload is avoided.

Germ-Plasm Dysplasia

Male germinal dysplasia offers quite a different problem than a simple germinal hypoplasia, for there is a fundamental defect in the germ plasm so that a part of or all the germinal epithelium becomes incapable of reproducing other than defective spermatozoa. At times, an alteration occurs in the ratio of normal and abnormal spermatozoa in different samples from the same person, a finding that is apparently due rather to differences in the rate of spermatogenesis in the healthy and abnormal elements of the germinal epithelium than to any fundamental improvement in the germ plasm as a whole. The diagnosis of germ-plasm dysplasia depends on the examination of properly stained smears of semen and the determination of the type and ratio of spermatogenic abnormalities. Even the use of testicular biopsies is inadequate for the diagnosis of a dysplasia, since the spermatozoa seen in a biopsy are cut in different planes, rendering the recognition of abnormalities of the mature spermatozoa literally impossible. As a result of the rather widespread failure to study adequately stained specimens of semen, the whole matter of germinal hypoplasia, dysplasia and asthenospermia has been badly jumbled.

Dysplastic germinal epithelium is frequently less capable of producing normal numbers of spermatozoa than normal germ plasm, and the association of hypoplasia and dysplasia is accordingly a common feature; although it carries with it an extremely unfavorable prognosis, one should remember that fertilization is always possible if any apparently normal spermatozoa are found in the ejaculate. If all spermatozoa are abnormal, even if they occur in normal numbers and are highly active, one need have no hesitancy in rendering a hopeless prognosis. When the growth potentialities of the germ plasm have been completely altered, there

is no more likelihood of benefit from any form of therapy than one would obtain by altering the growth potentialities of other tissues of the body.

In most cases of sterility, only a portion of the germ plasm is dysplastic, and accordingly millions of normal appearing and acting spermatozoa are usually mixed in the ejaculate along with imperfect spermatozoa. Clinical experience with human and animal semen examinations suggests that the agent or agents responsible for the visible effects on a portion of the germinal epithelium also act on the more normal appearing elements to reduce their fertilizing ability according to the extent of damage. This damage and the fertilizing potentialities of a sperm population are best estimated on the basis of the extent of observed abnormalities, together with a consideration of the rate of spermatogenesis. In most cases of sterility resulting from germinal dysplasia, there exists a wide variety of bizarre abnormal forms, which have resulted from variations affecting either the nucleus or the acrosome. Since, in structurally abnormal spermatozoa, the nucleus and acrosome are usually involved, it follows that if a sperm population is broken down into four groups (Fig. 1), one containing normal appearing spermatozoa, another presenting nuclear abnormalities, a third with acrosomic defects and a fourth containing the miscellaneous assortment of other abnormalities, one will obtain a fairly reliable idea of the constitution of the sperm population and, thereby, a basis for estimating fertilization potentialities. The latter is far from an exact science, but is nevertheless an indispensable part of any sterility diagnosis that aims at reliability.

Asthenospermia

In other cases, there is evidence that the ability to fertilize the ovum is diminished, in spite of the normal appearance of the sperm population. The motility of such populations may or may not be impaired, and the semen examination alone provides an extremely poor means for arriving at a valid diagnosis. This condition, commonly known as asthenospermia, results from a variety of etiologic factors. Patients with a low basal metabolic rate and those presenting a chronic prostatitis furnish good examples, for, as in other somatic conditions, there is often clinical evidence of impaired fertility without structural alterations in the spermia or faulty spermatogenesis. One must thus recognize the existence of cases in which functional defects without a demonstrable lesion lower the fertilizing ability of the sperm population, but the diagnosis is hardly justified unless a careful examination fails to reveal the presence of significant spermatogenic abnormalities, and unless the anamnesis and the somatic examination together with

general laboratory studies show the presence of some factor that might reasonably impair the vitality of the spermatozoa.

Relation of Male and Female Sterility Studies

The diagnosis, prognosis and treatment of male and female sterility are so interdependent in vari-

expected ovulation (Fig. 2). No arbitrary means of calculating the ovulation date will suffice in sterility work because of the marked variation of ovulation time and the extreme brevity of the period during which fertilization is possible. As a result, when there is an indication for a severe restriction of sexual relations, there must be a

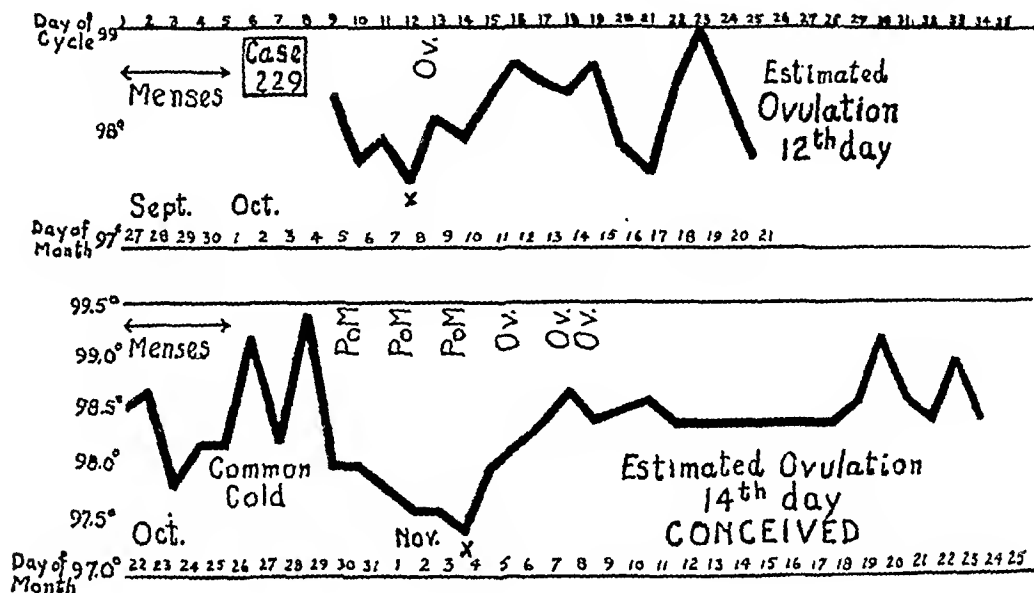


FIGURE 2. Case 229.

This chart records the basal body temperatures and vaginal smears during two menstrual cycles (actual menstruation indicated by arrows) in a twenty-six-year-old woman who had been married for seven and a half years. No contraceptives had been used, but conception had never occurred. The woman was normal. The husband, who was thirty years old, presented severe germinal hypoplasia (3700 spermatozoa per cubic millimeter) and severe germinal dysplasia (56 per cent pathologic spermatozoa). Conception occurred at the first timed intercourse after four weeks of sexual inactivity.

X = sexual relations; PoM = postmenstrual type of vaginal smear; Ov = ovulatory type of vaginal smear.

ous aspects that little constructive work on the husband is to be expected from studies not closely related to studies on the wife. For example, in germinal hypoplasia and dysplasia, a restriction of relations to the fertile phase of the menstrual cycle is often highly desirable, and accordingly it becomes necessary to subject the wife to routine objective tests and to estimate each month the date of

careful timing to the fertile phase, or the chance of fertilization may be missed altogether.

SUMMARY

The various causes of male sterility are discussed, and the need for closely correlated studies of husband and wife is emphasized.

146 Chestnut Street

MEDICAL PROGRESS

WOUND HEALING*

ARTHUR D. HOLMES, PH D †

BOSTON

WOUND healing has occupied the attention of man through the entire human era, for without doubt the prehistoric man received wounds and tried to cure them. In fact even animals adopt procedures for treating wounds. The muskrat caught in a steel trap amputates his foot and applies his own treatment for healing the wound. And, who has not seen a dog lick his wound in an attempt to allay pain and promote healing?

During human existence literally thousands of substances have been suggested for promoting wound healing, but obviously it is impossible within the scope of this paper to cover all the materials that have been recorded in the literature for stimulating the growth of new tissue in wounds. Accordingly attention will be confined to a number of factors and materials that have been the subject of investigations reported during recent years. These are the influence on wound healing of diet, hydrogen ion concentration, zinc peroxide, maggots and urea, sulfhydryl compounds, sulfonamides, gramicidin and penicillin, tissues and tissue juices, vitamins and cod liver oil. An attempt will be made to discuss these topics as separate entities, but it will be seen that there is frequent overlapping. For instance, it is extremely difficult, if not impossible, to eliminate completely the influence of the diet on wound healing when attempting to evaluate the therapeutic activity or value of substances such as sulfonamides or cod liver oil, for promoting the growth of tissues. In a measure the factors and substances discussed may be divided into two classes: those used for inhibiting the growth of or killing organisms found in wounds, and those used for stimulating tissue growth. But this classification cannot be followed completely since some of the factors and materials do not belong entirely in either group.

DIET

Wound healing obviously requires the growth of new tissues, which involves the production of

protein characteristic of the subject. Carbohydrates and fats are also essential for satisfactory metabolism in the wounded as well as in the normal individual. Thus the question of the influence of the diet on wound healing has been a subject of much interest to investigators.

Harvey and Howes,¹ in studying the effect of high protein diet on the velocity of growth of fibroblasts in the healing wound, found that during the latent period it had no effect, but once growth was started the velocity of healing was distinctly increased by a high protein regime. As a consequence the maximum strength of the healing wound was reached two days earlier than with a standard diet. Thompson, Ravdin and Frank,² in experiments with dogs, demonstrated a relation between hypoproteinemia and the disruption of surgical wounds and showed that the hypoproteinemic dog is frequently incapable of wound fibroplasia. Burrows³ states that the connective cells except where they are very closely packed together in a wound cannot destroy the fibrin, but they do take fats, serum proteins and evidently other substances from the blood clots.

Rhoads, Fliegelman and Panzer⁴ promoted wound healing in hypoproteinemic dogs by injecting large amounts of acacia, which they assume tends to mobilize protein for utilization but they caution that this treatment is not justifiable for treating human wounds. Clark⁵ has assembled data concerning the effect of the principal ingredients of the diet on wound healing. Four groups of three dogs of the same size, age and condition were fed a mixed, a carbohydrate, a protein and a fat diet for three days, after which they were anesthetized and wounds were made in their backs. The experimental diets materially influenced the length of the quiescent period of wound healing. There was no quiescent period for the protein fed dogs, the period was three days for the carbohydrate fed dogs, four days for the dogs that received the mixed diet, and six days for the fat fed dogs. The effect of the diet on the length of the quiescent period was greater for small than for large wounds, but in all cases the scar was one quarter the size of the original wound.

Reprints of articles in this series are not available for distribution but the articles will be published in book form. The current volume is *Medical Progress Annals*, Vol. III, 1947 (Springfield, Ill. no. 3; Charles C. Thomas Company, Inc., \$5.00).

*From the Research Laboratories E. L. Patch Company, Boston.
†Formerly director of research E. L. Patch Company now research professor of chemistry Massachusetts State College, Amherst.

A number of investigators have commented on the importance of the diet during the treatment of various lesions. Whipple⁶ states that a protein deficiency retards but a high-protein diet accelerates wound healing. He also noted that a high-fat diet prolongs the period of repair in wounds. Weil, Whitaker and Rusbridge⁷ state that a high-protein, high-vitamin diet should be used in the treatment of wound cases. Holman⁸ has carefully observed the influence of the diet in preoperative and postoperative care of the surgical patient, and recommends a high-calorie, high-vitamin diet for two weeks preceding an elective operation. Strumia, Wagner and Haylar,⁹ in discussing the management of shock and treatment of burns, emphasizes that a high-calorie high-polyvitamin diet is indicated for promoting the growth of tissue in burned areas.

It is generally agreed that for continued health and bodily well-being the human dietary should supply adequate amounts of several vitamins, but only three, vitamins A, D and C, will be considered at this time. For convenience vitamins A and D will be considered together.

Vitamins A and D

Roegholt¹⁰ did not find that vitamin A deficiency affected the rate of healing in epithelial wounds. Saitta¹⁰ reported that the rate of healing of epithelial wounds on animals that had received a vitamin-A-deficient diet for sixty-six days did not differ from that of controls. When the vitamin-A-deficient diet was continued for one hundred and five days the wounds remained unhealed, became infected, and the animals died, but when wounds were painted with a vitamin A extract they healed in thirteen days. Lauber¹⁰ found that pretreatment of rats with vitamin A did not affect the rate of healing in wounds subsequently produced. However, oral administration of the vitamin following the infliction of skin wounds produced remarkable acceleration in healing. Some lesions healed in nine days, as compared with eighteen to twenty-five for controls. When 200 units per day was administered there was no noticeable effect on the rate of healing. When 40,000 units was administered, however, healing required thirty-six to fifty-two days. Bailey¹¹ believes that vitamin A deficiency decreases the effectiveness of the epithelial barrier to infection. Tammann¹⁰ found that overdosage with vitamin D delayed wound healing. Lauber¹⁰ failed to produce any effect on the healing time in rats by foretreatment or concurrent treatment with varying doses of vitamin D, including overdosage, but thinks that these results do not afford safe conclusions for application to human therapy.

Vitamin C

Wolbach and Howe¹² characterize scurbutus as the inability of supporting tissues to produce and maintain intercellular substances, and believe that such failure is due to an inadequate supply of ascorbic acid. Smith and McConkey¹³ found that scorbutic guinea pigs were liable to develop duodenal ulcers. Experimental wounds in such animals healed completely with no abnormalities when the animals received canned tomato juice daily, but no healing occurred in wounds of similar animals receiving no vitamin C supplement, and coincidentally 80 per cent of the animals developed ulcers of the duodenum.

Whipple⁶ concludes that vitamin C deficiency prolongs the healing process, and he suggests that even if peptic ulcer patients have no vitamin C deficiency when admitted to the hospital, only four days of strict ulcer dietary regime will cause them to develop this deficiency. Davidson¹⁴ found that patients receiving an ulcer-producing (vitamin-C-deficient) diet developed deficiency disease, and emphasizes the necessity of including adequate accessory food factors in special diets to prevent development of deficiency diseases. Ingalls and Warren¹⁵ determined the vitamin C contents of the blood plasma of 20 patients with gastric or duodenal ulcers, 18 (90 per cent) of whom had low vitamin C values. They emphasize the importance of the clinician's being sure that his patients receive an amount of vitamin C adequate to promote wound healing. Holman⁸ found that a vitamin-C-deficient diet retarded the healing in 44 per cent of 70 patients and that ascorbic acid is essential for the synthesis and maintenance of intercellular supporting materials. He recommends that in elective operations, such as hernia, the patients receive generous amounts of ascorbic acid for two weeks preoperatively to ensure rapid healing of wounds. Lanman and Ingalls¹⁶ present evidence that even a partial vitamin C deficiency has important bearing in the treatment of surgical wounds and that administration of ascorbic acid to promote wound healing is indicated.

Hunt¹⁷ states that, as early as 1772, James Lind noticed a relation between scurvy (vitamin C deficiency) and delayed wound healing. He points out that vitamin C deficiency is particularly prevalent in patients with gastrointestinal diseases and that most wounds break down on about the tenth day, but that this condition may be eliminated by saturating patients with vitamin C. One thousand milligrams daily for three days produces saturation, and 100 mg. daily thereafter maintains it.

Lund and Crandon¹⁸ report that vitamin C reserves in the tissues or in the tissue cells, not the blood-plasma level, are the determining factor in healing. They examined 58 patients one year after operation and found that those with low preoperative blood plasma levels had a larger percentage of postoperative hernias after gall-bladder operations than did those with high levels. They recommend that patients with low reserves receive preoperative and early postoperative treatment with vitamin C.

Archer and Graham¹⁹ observe that following long periods of ill health or strict diet patients are likely to be in a subscurvy state. Thus many patients on a strict diet due to gastric or duodenal ulcers lack ascorbic acid in their body. Hence, for ulcer patients these authors recommend 1000 mg. of ascorbic acid for three successive days to saturate the body, and then a daily dose of 36 mg.

Platt²⁰ reports 4 cases of adult scurvy seen in private practice. One patient was a neurotic woman who had dieted; 3 were peptic ulcer patients on dietetic treatment. Administration of vitamin C from natural or artificial sources cured the scurvy that had resulted from the prolonged treatment with diets lacking vitamin C.

Hartzell, Winfield and Irvin²¹ report that a group of patients with clean wounds and apparently uneventful convalescence experienced disruption of wounds without warning and without apparent physical cause. The levels of plasma vitamin C and serum protein were low. The relation of these factors to poor wound healing cannot be overlooked. In discussing vitamin therapy in practice Vorhaus²² stresses the importance of vitamin C both before and after operation. Madison and Manwaring²³ have shown experimentally that vitamin C aids the body in defense against infectious diseases and a large dose increases antibody production.

Crandon, Lund and Dill²⁴ concluded from a study of human scurvy that total vitamin C deficiency causes failure of wound healing. Microscopically the tissues showed a lack of intercellular substance, but parenteral administration of vitamin C produced good healing and considerable intercellular substance within ten days.

In discussing the prevention of infection in wounds and burns, the Committee on Chemotherapeutic and Other Agents and the Committee on Surgery of the Division of Medical Sciences of the National Research Council²⁵ state that a reduction of vitamin stores, especially vitamin C, interferes with normal wound healing, and they recommend the daily oral administration of 75 mg of ascorbic acid until recovery is complete.

The significance of vitamins applied locally will be considered later, but the data cited above indicate the importance of a carefully selected dietary in the treatment of accidental or surgical wounds, particularly if they are extensive.

HYDROGEN-ION CONCENTRATION

Practically everyone has at some time experienced definite discomfort when sweat, salt, soap, acid or some other substance has entered his wound. However, very few have associated this unpleasant experience with a change in the hydrogen ion concentration of the wound, but a number of investigators have determined the hydrogen-ion concentration of wounds subjected to different types of treatments.

Messer and McClellan²⁶ measured the pH of healing wounds by placing contact electrodes in them. In all cases the fluctuations in pH followed roughly the clinical conditions of the wounds; progressive healthy healing was accompanied by consistent increase in alkalinity, whereas failure of healing was followed by fluctuations toward acidity. Wounds that healed rapidly with pinkish granulation tissue and flat, undistorted scar tissue showed an alkalinity of pH 7.4. Messer and McClellan believe that excess alkalinity is a factor in bacteriostasis and wound healing.

Hashizume²⁷ is not in agreement with this conclusion. He determined the pH of the secretions of infectious and noninfectious wounds of man under various conditions and found that regardless of favorable or unfavorable conditions for wound healing, the pH quickly approached that of the tissue or blood if the wound surface was exposed to the air. He concludes that change in pH does not parallel the course of healing but is correlated with the rate of escape of carbon dioxide. In his extensive studies of the value of chloramine-T for promoting wound healing, Carrel²⁸ observed that it was nonirritating to the tissues. Chloramine-T U.S.P. (1:20)²⁹ must be alkaline and thus has a pH in excess of 7.0.

Reimers and Winkler³⁰ produced acidosis in dogs by the administration of ammonium chloride, and found a definite shortening of the period of wound healing.

Robinson³¹ states that 2 per cent solutions of ammonium bicarbonate (pH 7.7) promote healing of such conditions as chronic osteomyelitis, stitch abscesses, chronic varicose ulcers and lacerations, with the formation of little scar tissue and in some cases return of the hair to the surface of the wound.

Rohde³² reports that chronically inflamed granulation tissues tend to have an acid reaction, with pH values ranging from 6.8 to 7.1. Arcy³³ found that pain in aseptic wounds was related to the local

acidity. Injections of buffered acid phosphate solution are painful but those of buffered alkaline phosphate solution produce no pain. He suggests that the strong pain of inflamed wounds is related to local acidity; thus pain in abscesses, ulcers and allied conditions can be relieved by the injection of buffered alkaline phosphate solution. Human experiments showed that pain began at pH 7.2 and increased progressively until at pH 5.9 it was unbearable.

The results of these studies are practically unanimous in indicating that a pH in excess of 7.0 is desirable for enhancing the patient's comfort and providing a condition favorable for rapid tissue growth.

ZINC PEROXIDE

For many years it has been recognized that rapid oxidation greatly inhibits the activity of pyogenic bacteria found in wounds. Hydrogen peroxide has been very extensively used, but during recent years considerable attention has been given to the value of zinc peroxide as an oxidizing agent for treating wounds.

Bliss, Long and Smith³¹ applied zinc peroxide locally and found it highly active in controlling infection due to *Clostridium oedematiens*; when used intramuscularly in the treatment of *Cl. tetani* infections in mice, it was much more effective than sulfathiazole. They found wide variation in the effect of zinc peroxide in different types of infections. It produced excellent results in the therapy and prophylaxis of *Cl. tetani* and *Cl. oedematiens* infections but was far below sulfadiazine in controlling *Cl. septique* and was practically worthless against *Cl. welchii*. On the other hand, Johnson and Meleney,³² who tested sterilized medicinal-grade zinc peroxide on a variety of organisms, report that *Cl. welchii* and *Cl. tetani* were the most susceptible to its action; hemolytic streptococcus, pneumococci, *Cl. histolyticum*, *Cl. sporogenes*, *Cl. novyi* and *Cl. sordellii* were less sensitive; and *Streptococcus viridans*, *Staphylococcus aureus*, *Escherichia coli*, *Proteus vulgaris* and *Pseudomonas pyocyaneus* were relatively resistant.

Friel³⁶ studied the value of ionized zinc in the treatment of suppurating surfaces. Layers of gauze soaked in sterilized solution of zinc sulfate in gelatin were laid on the raw area, a positive electrode was kept in contact by a bandage, and at intervals cultures were made from the surface. The advantage of the zinc ionization is the speed with which suppuration may disappear. Friel believes that suppuration ceases because zinc albuminate is a bad culture medium for micro-organisms and causes no irritation to the wound. Gurewitsch³⁷ treated 15 patients with indolent ulcer by placing

zinc peroxide paste on the ulcer, covering it with a gauze pad saturated with saline and applying a positive electrode.

Meleney³⁸ recommends zinc peroxide for prevention of the growth of organisms in grossly contaminated wounds, particularly around the mouth, colostomies, anus, fistulas and pilonidal cysts where anaerobic organisms are known to be involved. He recommends its use as a prophylactic against infection of the peritoneal cavity after appendectomy or abdominal resections of the bowel, and states that if streptococci or *Cl. welchii* is present in a closed wound it should be opened and zinc peroxide applied. He further states that zinc peroxide acts best if it is kept wet, and that, although tissue fluids will activate it, distilled water or 2 per cent polyvinyl alcohol will keep it wet longer.

An editorial states that zinc peroxide has been used successfully in the dangerous human bite, perirectal and deep pelvic abscesses, and gangrene, and that combined with glyceryl monostearate and peanut oil as a base it is a powerful therapeutic weapon against all anaerobic bacteria and hemolytic streptococci.³⁹

Noel and Lynn¹⁰ report the variability of results obtained from zinc peroxide therapy. They conclude that no true substance of this composition exists, and that the commercial products are probably chemical or physical combinations of zinc oxide with hydrogen peroxide, their value being proportional to the amount of available oxygen, established by assay. The rapid drying of pharmaceutical preparations, previously a serious handicap in practice, has been largely overcome by the incorporation of sorbitol, but mannitol does not produce such satisfactory results.

Although numerous investigators have found freshly prepared zinc peroxide effective for killing pyogenic bacteria in wounds, it leaves a zinc oxide residue; also it would doubtless deteriorate in preparations stored for considerable periods.

MAGGOTS — ALLANTOIN AND UREA

It was frequently observed during World War I that wounds that had become infested with maggots healed more satisfactorily than those that had received more prompt attention. However, this was not an original observation, for some three centuries ago Ambroise Paré⁴¹ was aware of the beneficial results of live maggots in wounds. Also a century or more ago Larrey⁴¹ noted that the wounds of Syrian soldiers were benefited by the presence of maggots, and that the latter consumed only dead and decomposed tissue and did not touch live tissues. Keen⁴¹ says that during the Civil War wounds were frequently infested with maggots, but they never caused harm and

were frequently beneficial Baer⁴² found that maggots removed fragments of bone and tissue sloughs,—an asset in wound healing,—caused wounds to become alkaline, thus inhibiting the growth of pathogenic bacteria, and contributed some subtle biochemical effect within the wound. He also found that maggot treatment of open tuberculous abscesses, with or without infection, was surprisingly effective. Messer and McClellan,⁴³ in studying the functions of surgical maggots in wound healing, observed that osteomyelitis wounds treated with blow fly larvae showed rapid cleansing, pinkish granulation tissue and a flat, undistorted scar.

Robinson⁴³ noted that the excretion of maggots contained allantoin, and when it was used for treating experimental wounds, results similar to those produced by maggots were obtained. However, nearly a quarter of a century earlier Macalister⁴⁴ had treated chronic ulcers with a solution of allantoin and obtained healing with rapid granulations. He also successfully used allantoin internally for treating gastric and duodenal ulcers. In later investigations Robinson⁴⁵ found that the maggot excretion also contained urea, and when this was tested on human wounds it was found to possess definite healing value.

Holder and MacKay⁴⁶ treated 139 cases with urea without any deleterious effects and obtained their best results with chronic ulcers. They found that urea was nontoxic and harmless, a solvent of dead tissue, dried secretions and other materials that hinder healing, and bacteriostatic in strong solutions. In a later paper they⁴⁷ noted that hypertonic solutions of urea may be painful to denuded tissues, and suggest that isoamyl hydrocupreine be combined with the urea for its local anesthetic action. Millar⁴⁸ states that urea is cheap and readily available, does not irritate tissue, has some antiseptic value, causes no systemic reactions, and is very effective in eliminating odors, particularly the peculiar penetrating fetor of sloughing cancer. Robinson⁴⁹ found that urea stimulates the growth of granulation tissue and the development of capillaries, is easily prepared for use by adding to cold, sterile distilled water, and is effective in the treatment of such purulent conditions as varicose and diabetic ulcers, carbuncles, suppurating x-ray burns, infected heat burns, intraoral infections, osteomyelitis and skin infections. Foulger and Foshay⁴⁹ used urea successfully in 20 cases of purulent otitis media that had failed to respond to other medicaments. The discharge lost the foul odor, became serous, and in three to six days ceased, even though it originally contained hemolytic streptococci. Unfortunately the urea caused pain, which was controlled with morphine. Wilson⁵⁰ states that an

8 per cent solution of urea prevents the growth of *Esch coli*. Symmers and Kirk⁵¹ successfully treated chronic staphylococcus infection with urea. Wilson reports that small amounts of urea added to nutrient mediums have a distinct effect on *Esch coli*, *Eberthella typhosa*, *Salmonella enteritidis*, *Ps pyocyanea* and Friedlander's bacillus. Olson, Slider, Clark and MacDonald⁵² found that urea retards the rate of epithelialization of open skin wounds of rabbits but stimulates the rate and extent of granulation tissue.

The investigators cited above are apparently in complete agreement that urea is a valuable material for promoting wound healing, particularly for removing debris and necrotic tissues. However, to be effective, concentrated solutions (30 per cent or more) must be used, and in some cases these cause the patient discomfort and sometimes require sedation.

SULFHYDRYL COMPOUNDS

In considering the effect of sulfhydryl compounds on wound repair, Riley⁵³ is of the opinion that they stimulate growth by mitosis. Reimann and Hammett⁵⁴ report treating aged persons with varicose, decubitus and trophic ulcers with thioglucose solution, 1:10,000, as a wet dressing and thus stimulating granulations and epithelial growth. However, this product also promotes bacterial growth, which in turn inhibits healing. Consequently sulfhydryl solutions should not be used for more than twenty-four hours, with intervals of two or three days between treatments. Pierce⁵⁵ thinks that sulfhydryl compounds are of great importance in tissue growth and are best applied to burns as compresses. Most patients complain of pain when a sulfhydryl solution is applied to the burned area but this does not persist over one or two hours. Reimann⁵⁶ reports using a sulfhydryl preparation on decubitus and pressure ulcers, one of which had not healed after six months' treatment with other preparations. Para-thiocresol, 1:10,000, produced healthy granulations within forty-eight hours. However, treatment was stopped for three days, during which time physiologic sodium chloride solution was applied, after which the *p*-thiocresol treatment was repeated. Sulfhydryl solutions must always be made fresh, and they have a disagreeable odor. Fitzhugh⁵⁷ in studying the effect of sulfhydryl compounds in otolaryngology found that they could not be used in the presence of marked, purulent exudate. After granulation has started *p*-thiocresol can be applied and will promote epithelial growth. When applied to postauricular incisions, healing occurs in three or four days.

A number of investigators have shown that sulfhydryl compounds possess unusual value for stimulating tissue growth. Unfortunately they

also stimulate the growth of organisms present in wounds, and consequently in the treatment of lesions they should be used alternately with other types of medication.

SULFONAMIDES

Although sulfanilamide was synthesized thirty years or more ago, it is only within the last six or eight years that attention has been given to the remarkable bactericidal power of the sulfonamides. Even so, the present volume of literature concerning them is so extensive that only a limited number of investigations can be included.

According to Buttle,⁵⁸ the value of sulfonamides in the treatment of human wounds is due to their ability to inhibit bacterial growth with little or no harmful effect on the phagocytic cells. Huang and Sia,⁵⁹ Fuller and James,⁶⁰ Colebrook and Francis,⁶¹ Buttle⁵⁸ and others report that sulfanilamide applied to a wound inhibits growth of the hemolytic streptococcus and of the gas-gangrene organisms, particularly *Cl. welchii*.

Most of the deaths from infection⁶² in World War I were due to hemolytic streptococci and gas-gangrene organisms. Sulfanilamide is particularly effective against these bacteria. Fuller and James⁶⁰ recommend that the first dose of 1.5 gm. be placed in the wound as soon as possible. Delay is dangerous. If several hours have elapsed, the amount administered orally in the first doses should be increased. Beginning two hours after the first dose intact 0.5-gm. tablets should be given at four-hour intervals. Prophylaxis must be continued for at least four days to counteract hemolytic streptococcus infections which may occur in the hospital. Coated tablets used to secure prolonged retention of the drug do not offer any advantages. Colebrook and Francis⁶¹ studied the effect of sulfanilamide powder on sixty-two superficial wounds infected with hemolytic streptococci. The organism disappeared from the wounds within three or four days, but infections with Group D streptococci, staphylococci, *Prot. vulgaris* or *Ps. pyocyanea* were resistant to local sulfanilamide treatment. Jackson and Collier⁶³ recommend the local use of sulfanilamide in peritonitis and conclude that it causes no injury to the peritoneal surfaces. Jensen, Johnsrud and Nelson⁶⁴ treated forty-one wounds associated with compound fractures with 5 to 15 gm. of sulfanilamide. The wounds healed by first intention in all but 2 cases, but before the use of sulfanilamide the infection rate was 27 per cent. Blood assays showed that after local treatment the maximum concentration of sulfanilamide in the blood occurred in eighteen hours. Purdie and Fry⁶⁵ administered a total of 94 gm. of sulfanilamide to a patient with several discharging wounds

containing hemolytic streptococci and *Esch. coli* that had remained unhealed for three years, in spite of operative procedures and actinotherapy. Four days later the wounds discharged less, in twenty-three days they were nearly healed, and after forty-four days they were completely healed. In discussing compound fractures complicated with gas-gangrene, Bohlman⁶⁶ states that sulfanilamide has a specific effect on gas bacilli, but cautions that conservative surgical principles must be combined with its use. Gibbon and Hodge⁶⁷ are of the opinion that sulfanilamide should be employed locally and orally in all patients with traumatic wounds.

In comparing the absorption of the various sulfonamides, Hawking⁶⁸ found that 0.2 gm. of sulfanilamide inserted in an experimental wound in a guinea pig's thigh was absorbed in less than twenty-four hours; sulfathiazole in four or five days, and sulfapyridine in seven to ten days. Sulfanilamide placed in one end of an 8-cm. wound produced high concentration at the distal end in two hours, sulfathiazole and sulfanilylguanidine high concentration in two to six hours, sulfadiazine moderate concentration in six to twenty-four hours, and sulfapyridine low concentration in twenty-four hours.

From their experience in the Libyan campaign, Mitchell, Logie and Handley⁶⁹ emphasize both oral and local administration of sulfonamides, since their patients so treated were fitter and showed less local sepsis than did controls. They suggest applying 15 gm. of sulfanilamide immediately to the wound and 15 gm. more after operation. Twenty-seven grams is administered orally to the patient in six days.

Numerous investigators have recommended the local application of sulfonamides to various types of wounds. Miles⁷⁰ says that even in the presence of pus they reduce streptococci, staphylococci, coliform bacilli and sporebearing anaerobes when applied locally to wounds, and recommends both local and oral administration of sulfathiazole. Griswold and Antonie⁷¹ recommend the local implantation of sulfanilamide in the abdomen for perforated peptic ulcers, perforated appendicitis or gunshot wounds, or when the lumen of the gastrointestinal tract is opened; and the Committee on Chemotherapeutic and Other Agents and the Committee on Surgery of the Division of Medical Sciences of the National Research Council⁷² recommend the liberal application of crystalline sulfanilamide to all wounds as soon as possible after they are incurred.

Although it is generally recognized that sulfonamides are used in the treatment of wounds for their bactericidal activity, a number of investiga-

tors have referred to their influence on cell growth. Livingston,⁷² Mayo and Miller,⁷³ Guerry and Putney⁷⁴ and Thompson, Brabson and Walker⁷⁵ think that sulfanilamide and sulfathiazole stimulate tissue growth. Kev, Frankel and Burford.⁷⁶ Kev⁷⁷ and Key and Burford⁷⁸ believe that sulfanilamide does not seriously interfere with wound healing. Goldberger⁷⁹ states that wound healing is not appreciably inhibited by the sulfonamides. On the other hand, Bick⁸⁰ reports that the local application of sulfonamides to wounds retards healing by 50 per cent and promotes excessive cutaneous scarring. Lyons and Burbank⁸¹ believe that local applications of sulfanilamide delay wound healing.

Fleming,⁸² Kolmer and Brown,⁸³ Lockwood⁸⁴ and others have found that such materials as thick suspensions of bacteria, peptones, dead streptococci and tissue residues inhibit the bacteriostatic action of sulfanilamide. Rubbo and Gillespie⁸⁵ found that as little as 1 part of *p*-aminobenzoic acid reverses the bacteriostasis of 26,000 parts of sulfanilamide, and Weil, Whitaker and Rusbridge⁷ report that novocain is an inhibitor and is contraindicated for cases in which sulfathiazole is to be used.

Jones⁸⁶ recommends that a cod-liver oil emulsion containing 5 per cent sulfanilamide be used routinely for wounds, but Locatelli and Bowden,⁸⁷ Fitch⁸⁸ and Pillsbury, Wammock, Livingood and Nichols⁸⁹ say that an emulsion with an oily base retards and reduces the activity of sulfanilamide.

Mueller⁹⁰ believes that sulfanilamide must be sterilized before being placed in the abdominal cavity. Thompson, Brabson and Walker⁷⁵ are of the same opinion and recommend heating the drug in test tubes at 120°C. for half an hour. On the other hand, Key and Lembeck⁹¹ think this unnecessary, since pathogenic organisms will not be carried into the wound in the sulfanilamide powder, and Herrell and Brown⁹² hold that there is no necessity for sterilizing sulfanilamide or sulfathiazole powder before direct application to an open wound.

Very recently a number of investigators have described undesirable side reactions of varied nature and intensity which have been noted following the administration of the sulfonamides. In the case of sulfanilamide, Weitzen⁹³ has observed angular and curvilinear distortions, disturbed distance perception and micropsia in his patients; Higgins⁹⁴ reported aphasia and stammering on the third day of sulfanilamide medication; Pearson and Burnstine⁹⁵ have called attention to a series of cases of psychoses; Garvin⁹⁶ described a patient who became irrational and confused after a single dose of sulfanilamide; Ottenberg⁹⁷ reported death following toxic psychosis; Waugh⁹⁸ observed 1 case of peripheral neuritis among 650 patients;

Janet⁹⁹ commented on a case that developed neuritis of the arm and thorax; Ornstein and Furst¹⁰⁰ described a case of dystrophic gait and patchy distal hypesthesia; Fisher and Gilmour¹⁰¹ noted encephalomyelitis; Bucy¹⁰² observed toxic optic neuritis after a single 0.3-gm. tablet of sulfanilamide and Blankstein¹⁰³ reported transitory myopia.

Similar reports appear in the literature relative to the undesirable effects that develop after the administration of sulfathiazole. For instance, Weinberg and Knoll¹⁰⁴ noted a syndrome resembling amyotrophic lateral sclerosis; Stiles¹⁰⁵ called attention to hypersensitivity to even small doses of the drug; Finland, Peterson and Strauss¹⁰⁶ emphasized that such complications as drug fever, rash and granulocytopenia may follow its ingestion; Penner and Horack¹⁰⁷ reported transient renal complications following its administration; Loewenberg, Sloane and Chodoff¹⁰⁸ found at autopsy concretions in the kidneys, ureters and bladder of a case so treated; Cutts, Burgess and Chafee¹⁰⁹ reported a 10 per cent death rate and nitrogen retention in a series of patients who received the drug; Hoyne and Larimore¹¹⁰ observed gangrenous pharyngitis and laryngitis, focal membranous tracheitis, focal hemorrhagic bronchopneumonia and swelling of the myocardium, liver and kidneys at autopsy following death attributable to the ingestion of sulfathiazole; and Lederer and Rosenblatt¹¹¹ commented on the pathology in 4 cases in which death was attributable to this substance. Evidence published by Lyons and Balberor¹¹² indicates that approximately one third of all patients develop a sensitivity to sulfonamides sufficient to interfere with their subsequent use. Gallagher¹¹³ says that this type of sensitivity may persist for at least two years. Little¹¹⁴ reports the following abnormal conditions due to the use of sulfonamides: aphasia, stammering, toxic psychosis, peripheral neuritis, myelitis, optic neuritis, transitory myopia, meningeal signs, blindness and convulsions.

It is quite evident from this brief review of the literature of the sulfonamides that they have powerful bactericidal effect and are of great value to the surgeon and for wound treatment, but it is also evident that they possess undesirable qualities and can cause great damage unless administered under carefully supervised conditions.

GRAMICIDIN AND PENICILLIN

A number of years ago Dubos¹¹⁵ observed an unidentified sporebearing bacillus isolated from a sample of soil that rapidly killed pneumococci, streptococci and staphylococci when incubated with them at 37°C. but did not affect the virility or inhibit the growth of gram-negative bacilli. Dubos and Cattaneo¹¹⁶ prepared cell-free extract by re-

moving the protein precipitable at pH 4.5. The purified preparation is soluble and stable in alcohol, acetone, dioxane, pyridine and glacial acetic acid, and is insoluble in water, chloroform, sulfuric ether, benzol and toluol. The product contained 12.5 per cent of nitrogen, failed to give any test for proteins, and retained a bactericidal effect on gram-positive micro-organisms.

Hotchkiss and Dubos¹¹⁷ isolated from 100 gm. of crude material approximately 5 to 15 gm. of crystalline gramicidin, which crystallizes from acetone as characteristic spear-shaped, colorless platelets with a melting point of 228-230°C., found that 1 microgm. of gramicidin administered intraperitoneally protects a large percentage of mice infected intraperitoneally with 10,000 fatal doses of virulent Type I pneumococci, but 0.3 mg. administered intraperitoneally will kill mice, and smaller quantities will cause marked toxic reactions. Both tyrocidine and gramicidin are highly toxic when injected into the blood stream, but exhibit little toxicity when applied locally, as by the subcutaneous, intramuscular or intrapleural route. Christensen, Edwards and Piersma¹¹⁸ isolated the alcohol-soluble bactericidal material synthesized by *Bacillus brevis*. They are of the opinion that gramicidin is a polypeptide, and that its specific activity does not reside solely in these amino-acid residues.

Herrell and Heilman¹¹⁹ used the crude bactericidal substance obtained from a soil bacillus for bacteriological and clinical studies of gramicidin. Francis¹²⁰ believes that substances like gramicidin and penicillin can be used for the control and treatment of infections due to sulfonamide-resistant streptococci, and his experiments in vitro show that these streptococci are easily controlled by gramicidin. In their study of the effect of gramicidin administered orally to mice, Weinstein and Rammelkamp¹²¹ found it without effect on *Lactobacillus acidophilus*, whereas very small amounts had a bactericidal action on this bacillus in vitro. In evaluating the therapeutic activity of gramicidin one should not overlook the conclusions of Herrell and Brown,¹²² who note that recent observations concerning its hemolytic effect render it unsafe for general use. If its hemolytic property can be removed and its bacteriostatic effect preserved, an entirely new approach in the treatment of streptococcal infections may be developed.

In 1929, Fleming¹²³ found that a mold that appeared in laboratory bacterial cultures resembled *Penicillium rubrum*. The mold when grown on nutrient broth produced a very powerful antibacterial substance, which he named "penicillin." Its inhibiting action was very marked on pyogenic cocci and diphtheria bacilli, but was without action in colon, typhoid and influenza bacilli. A 1:800

dilution of the filtrate completely inhibited *Streptococcus pyogenes*, but did not inhibit the growth of *Haemophilus influenzae*.

Abraham et al.¹²⁴ have adopted as an arbitrary unit of antibacterial activity the amount of penicillin dissolved in 1 cc. of water, which gives the same inhibition as the standard. Material used in human therapeutic tests usually contains 40 to 50 units of penicillin per milligram. The administration of penicillin by mouth is complicated by the fact that it is rapidly destroyed by acid, and serious losses are to be expected in the stomach. These authors cite a case of local infection with hemolytic streptococci resistant to large doses of sulfanilamide and to moderate doses of sulfapyridine that improved greatly by treatment with penicillin. They report a case of corneal ulcer treated with a 1:5000 solution of penicillin in normal saline solution, with no irritation but improvement of the ulcer. Penicillin combines the two most desirable qualities of a chemotherapeutic agent—low toxicity to tissue cells and powerful bacteriostatic action. Its bacteriostatic action is in no way interfered with by body fluids or pus and only to a limited extent by large numbers of organisms. In local applications it has given promising results. Abraham et al. consider that enough evidence has been assembled to show that penicillin is an effective type of chemotherapeutic agent and possesses properties unknown in any other antibacterial substance heretofore described. Miles⁷⁰ says that penicillin is powerfully antibacterial. It has no observable toxic effect on phagocytes in antibacterial concentrations, and the antibacterial effect is not inhibited in the presence of organic matter. Its action is apparently bacteriostatic and thus permits the defenses of the body to take adequate action against the invader.

Although gramicidin and penicillin possess very interesting qualities and have unusually high bacterial activity, they have not been extensively studied. In fact, as yet it is only with difficulty that either can be obtained for investigational purposes. Obviously, both must be carefully observed, particularly with respect to any harmful qualities that they may possess, before they can be generally used for treating human wounds.

TISSUES AND TISSUE JUICES

In Carrel's¹²⁵ opinion the initiation of healing depends on the presence of leukocytes in wound tissue. Therefore he prepared leukocytic extracts from the blood of chickens one or two years of age and found that they possessed the power of increasing the multiplication of fibroblasts in vitro and stimulating the growth of tissues in vitro. The leukocytes are capable of bringing growth-activat-

ing substances to tissue cells. Even dead leukocytes set free substances that promote cell multiplication.

Carrell prepared aqueous extracts of inflamed connective tissue, which doubled the growth of new tissue, and embryonic juices from embryo chicks, which greatly stimulated the growth of fibroblasts in vitro. He believes that the power of tissue juice to cause growth is probably due to the ease with which its proteins can be transformed into peptides by tissue ferments, and that embryonic juices do not act as hormones but take part in the synthesis of protoplasm. The exact nature of the nitrogenous compounds present in these juices used by the epithelial and connective tissue cells in the building up of protoplasm is not known. Embryonic tissue juice loses its growth promoting effect after it is shaken for several hours or heated to 65°C for a few minutes. Attempts have been made to isolate the growth promoting substances from embryonic tissue juices, but fractionate precipitation by alcohol, acetone and other substances does not cause separation. The growth activating materials always remain with the protein precipitate.

Arey²³ points out that it is extremely difficult, if not impossible, to evaluate properly the effect of substances applied to wounds because of the possible concurrent effect of irritating stimuli. In this connection, Carrell¹²⁵ states that a slightly irritating dressing, dry gauze, turpentine or a few staphylococci will stimulate healing by irritating the wound, whereas the same substances have never been observed to produce an increase in the rate of multiplication of fibroblasts in vitro. Ruth¹²⁶ found that even injecting distilled water into the wounds of frogs stimulated the rate of epithelial proliferation.

A number of investigators have found that certain tissues and tissue juices promote tissue growth and thus stimulate wound healing. However, more extensive studies are needed in this field before tissues or tissue juices can be generally employed for treating wounds.

VITAMINS

Although a score or more of vitamins or vitaminlike substances have been studied with respect to their importance in the diet, only two, vitamins A and D, have received much attention as regards their influence on wound healing when applied locally.

Lohr,¹²⁷ lost and Kochergin,¹²⁷ Hayashi,¹²⁷ Lohr and Treusch,¹²⁷ Horn and Sandor,¹²⁷ Zoltan,¹²⁷ and Drigalski¹²⁷ are all of the opinion that vitamins A and D applied locally stimulate wound healing. Sandor¹²⁷ concludes from his clinical experience that vitamin A alone expedites the reparative

process. McLaughlin¹²⁸ thinks that vitamin A is essential to cell growth, but Davson¹⁻⁷ is positive that vitamin A is not a factor in wound healing. Pyke¹²⁷ is of the opinion that vitamins A and D have no value in the treatment of wounds, and Brindaleone and Papper¹²⁹ believe that vitamin D is not effective in wound healing. Saitta¹⁰ applied irradiated ergosterol to wounds and healing proceeded half as fast.

Liuber and Rocholl¹²⁷ found that all vitamin salves were ineffective in healing experimental wounds on rabbits except for one which contained vitamin A and cholesterol. This accelerated healing by approximately 50 per cent. Drigalski¹²⁷ reports that guinea pig skin wounds treated with an ointment containing vitamin A healed better than when a vitamin A free ointment was applied, and believes that the epithelial protective vitamin A was the factor responsible for the better healing.

The number and extent of the investigations reported in the literature consulted are too limited to permit any final conclusion concerning the therapeutic activity of vitamins A and D when applied locally for the treatment of various types of lesions. However, the reports of the investigators cited above indicate that the majority believe that vitamins A and D applied locally to wounds stimulate granulation and epithelization.

COD LIVER OIL

It is not known when cod liver oil was first used for the treatment of wounds and burns, but the scientific literature of the past twenty five years contains many papers dealing with this subject. During the past seven or eight years Lohr¹²⁷ has conducted many investigations and has reported clinical observations with over 15,000 cases of wounds, ulcers and other skin lesions treated with cod liver oil. Kemmler,¹²⁷ Proto,¹²⁷ Lohr and Unger,¹²⁹ Drigalski,¹²⁷ Puestow, Poncher and Hammatt¹³¹ and others were of the opinion that cod liver oil accelerated the healing of experimental wounds produced on rabbits and guinea pigs. Brindaleone and Papper¹²⁹ treated experimental wounds over the thoracic vertebrae of groups of 107 day-old rats, although more rapid healing was obtained in vitamin A deficient animals when cod liver oil was applied daily, such therapy had no effect on the rate of healing in normal animals. In other words, cod liver oil appeared to be of benefit only in the presence of generalized or local vitamin A deficiency. None of the treated animals developed infection, but 20 per cent of untreated animals became infected, and local application was more effective than oral administration of cod liver oil for promoting wound healing. In treating compound

fractures, especially under war conditions, Agostinelli¹³² recommends reduction of the fracture and careful cleansing and disinfecting of the wound, followed by daily application of cod-liver oil, which he believes prevents infection and stimulates rapid healing.

Several investigators have assembled data concerning the absorption of cod-liver oil by wounds. Helmer and Jansen,¹³³ Eddy and Howell,¹³⁴ Hume, Lucas and Smith,¹²⁷ Amrhein,¹²⁷ Astrowe and Morgan¹²⁷ and others have demonstrated that the vitamin A and D content of cod-liver oil can be absorbed through the unbroken skin. Zoltan,¹³⁵ Tennent,¹²⁷ Steel,¹²⁷ Lohr,¹²⁷ Iost and Kochergin,¹²⁷ Stevenson,¹²⁷ Brandaleone,¹³⁶ Ingram,¹³⁷ Hughes¹³⁸ and many others have reported that cod-liver oil promotes the granulation and epithelization of surgical and accidental wounds, ulcers and various types of lesions. In view of the outstanding results that have been obtained from the treatment of a wide variety of lesions with cod-liver oil, a question naturally arose as to the factor or factors that caused the stimulation of healing. Lohr,¹²⁷ Hayashi,¹²⁷ Lohr and Treusch,¹²⁷ Horn and Sandor,¹²⁷ Getz,¹³⁹ Kemmler,¹²⁷ Sandor¹²⁷ and others apparently believe that the therapeutic value of cod-liver oil for wound healing resides in its vitamin content. Pyke¹²⁷ thinks that its value for wound treatment is probably due to its rancidity, which he considers a possible source of "active oxygen." Recently Brandaleone and Papper¹²⁹ have commented on the influence of cod-liver oil fatty acids on wound healing, and Pels Leusden and Derlich¹⁴⁰ found that the removal of fatty acids from cod-liver oil reduced its bactericidal power.

Some investigators believe that cod-liver oil definitely inhibits the activity of organisms that infect wounds. Iost and Kochergin¹²⁷ think that cod-liver oil has great value in the treatment of wounds, owing to its inhibitory effect on certain types of pyogenic organisms. Tumanskiy and Yatsevich¹²⁷ claim that it inhibits the growth of both streptococci and staphylococci. Drigalski¹²⁷ found that cod-liver oil inhibited the bactericidal growth of gas and sporeforming bacteria, and Lohr¹²⁷ describes its value for treating local pyogenic infections. In a study of the bactericidal and sporicidal action of cod-liver oil, Pels Leusden and Derlich¹⁴⁰ killed such organisms as staphylococci, hemolytic streptococci and *B. anthracis* by suspending the organism in cod-liver oil. Campbell and Kieffer¹²⁷ report that cod-liver oil has a definite inhibitory and bactericidal action on virulent tubercle bacilli, lepra bacilli and *Eberth. typhosa*. Banyai¹⁴¹ recommends it for treating cutaneous and genitourinary tuberculous lesions. He accelerated healing following the removal of

tuberculous epididymes, testicles and kidneys by its local use.

Since it is difficult and often impossible to apply satisfactorily liquid cod-liver oil to lesions or wounds of ambulatory patients, cod-liver oil ointments have been developed for this purpose. Lohr,¹²⁷ who has made a careful study of the healing properties of cod-liver oil, seems to prefer it in an ointment. Other investigators such as Zuelzer,¹²⁷ Thiel,¹²⁷ Seiffert,¹²⁷ Arendt,¹²⁷ Lauber and Rocholl,¹²⁷ Jenico,¹²⁷ Schaer,¹²⁷ Horn and Sandor,¹²⁷ Drigalski,¹²⁷ Zoltan,¹²⁷ Ingram¹³⁷ and Lucke¹²⁷ also report using cod-liver oil ointments for healing wounds and other lesions. Cod-liver oil ointment was used during the Finnish War after excision of wounds, in conjunction with the closed plaster technic and was considered the method of choice.^{142, 143} In a study of the healing value of commercial cod-liver oil ointments Hardin¹⁴⁴ treated a series of 346 cases with wounds and burns. He reported that cod-liver oil is sterile and bactericidal, does not harm delicate tissues, exerts a beneficial systemic effect, reduces toxicity of pus, forms a protective nonirritating layer over the wound, and possesses a unique stimulating effect on the granulation and epithelization of tissues. In an eight-year study of the value of a 70 per cent cod-liver oil ointment in surgery, Aldrich¹⁴⁵ treated surgical lesions, varicose ulcers, decubitus ulcers, abrasions, minor burns, indolent burns and anorectal wounds and obtained prompt and satisfactory healing. Wolferman and Adams,¹⁴⁶ after extensive experience with cod-liver oil ointment in the treatment of industrial wounds, say that it is essentially bacteriostatic and sterile, and a stimulant to granulation, epithelization and wound healing.

SUMMARY

Literally thousands of materials have been suggested for promoting wound healing, but in this review of the literature attention has been centered on the influence on wound healing of diet, hydrogen-ion concentration, zinc peroxide, maggots and urea, sulfhydryl compounds, sulfonamides, gramicidin and penicillin, tissues and tissue juices, vitamins and cod-liver oil.

High-protein and high-polyvitamin diets are recommended. Investigators have shown that depletion of vitamin stores, especially that of vitamin C, interferes with wound healing; thus a carefully selected dietary is important in the treatment of accidental or surgical wounds, particularly if they are extensive.

Studies of the hydrogen-ion concentration of wounds have shown that a pH in excess of 7.0

favors healing and a pH of less than 7.0 is usually accompanied by pain. Hence a pH in excess of 7.0 enhances the patient's comfort and provides for rapid tissue growth.

Zinc peroxide has been found to be effective for killing pyogenic bacteria in wounds, but it leaves a zinc oxide residue and is likely to deteriorate in preparations stored for a long time before use.

During wars it has been observed that maggots promote the healing of wounds. Urea is one product of maggot excretions. Investigators agree that urea is valuable for promoting wound healing, particularly for removing debris and necrotic tissue, but concentrated solutions must be used. These may cause discomfort, and sedation is often necessary.

Sulphydryl compounds possess unusual value for stimulating tissue growth, but they also stimulate growth of organisms in wounds, and it is necessary to alternate sulphydryl treatment with other forms of medication.

The sulfonamides have unusually high bactericidal activity and are particularly effective in combating organisms frequently found in wounds. They are of great value to the surgeon, but they possess undesirable qualities and can cause serious damage unless administered under carefully supervised conditions.

Gramicidin and penicillin possess great bactericidal activity, but they have not been extensively studied clinically and must be carefully observed, particularly regarding any harmful qualities that they may possess, before they can be generally used for treating human wounds.

Investigators have found that certain tissues and tissue juices promote tissue growth and stimulate wound healing, but more extensive studies are needed in this field before these materials can be generally employed in the treatment of wounds.

Of the score or more of known vitamins, only two, vitamins A and D, have received much attention regarding their influence on wound healing when applied locally. Although the reported investigations are too limited to permit final conclusions, they show that these vitamins applied locally to wounds stimulate granulation and epithelization.

The literature contains numerous reports concerning the value of cod-liver oil for treating various types of wounds; but it seems likely that it promotes healing only in vitamin-A-deficient animals. Hence, the vitamin content is the likeliest active therapeutic agent. Some authors believe that cod-liver oil definitely inhibits the activity of organisms that infect wounds.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28501

PRESENTATION OF CASE

First admission. A fifty-nine-year-old woman was admitted because of severe colicky pain in the right lower quadrant.

The patient had been well until approximately nine hours prior to admission, when she was awakened by sudden, severe, knifelike pain in the right lower quadrant, which made her "double up and cry out." This radiated to the right lower flank and right upper quadrant and was followed by nausea, vomiting and occasional chilly sensations. She had never had a similar episode in the past. There was no urgency, frequency, dysuria, diarrhea or constipation. Her physician gave her morphine and nitroglycerin, which temporarily relieved the symptoms, but these soon recurred. The patient had been taking 8 gr. of thyroid daily for more than four years, although no definite diagnosis of hypothyroidism seemed to have been established. Her basal metabolic rate was -21 per cent, but her physician did not regard her as typically myxedematous. She was very sensitive to mushrooms.

Physical examination revealed a well-developed, rather obese woman in moderate distress, who complained of severe right-flank pain. Examination of the lungs was normal. The heart was somewhat enlarged to the left, and the sounds were very distant and muffled. A puffing systolic murmur was audible at the apex. There were tenderness and spasm in the right lower quadrant, maximum over an area just below McBurney's point, and there was tenderness at the right costo-vertebral angle.

The blood pressure was 96 systolic, 70 diastolic. The temperature was 99, the pulse 52, and the respirations 20.

Examination of the blood revealed a white-cell count of 8800. The urine was cloudy, amber and acid in reaction and had a specific gravity of 1.016; the sediment contained innumerable red cells, occasional white cells and epithelial cells. A blood Hinton test was negative. In a flat plate of the abdomen the kidneys were normal in size, shape and position. There was a triangular area of

calcification at the level of the right ischial spine. An intravenous pyelogram was normal on the left; on the right there was slight dilatation of the calyces, pelvis and ureter down to the area of calcification.

Soon after admission the right ureter was catheterized, and x-ray films showed that the stone had been carried upward approximately 3 or 4 cm. above its previous position. On the fourth day after admission the stone was removed. During hospitalization, she received a course of sulfathiazole by mouth, totaling 10 gm. in seven days. She was discharged on the eighth hospital day.

Final admission (nine days later). On the day after leaving the hospital she developed a slight fever and a feeling of weakness and lethargy and was thought possibly to have the gripe. She was started on sulfathiazole by mouth. Physicians were changed several times. This resulted only in the discontinuation of sulfathiazole and the substitution of sulfadiazine and later of sulfanilamide. During the eight days after discharge she received 125 gm. of sulfathiazole, 65 gm. of sulfadiazine and 2 gm. of sulfanilamide. One week after discharge she began to feel very weak and tended to sleep most of the time. At times she did not recognize people and did not respond well to stimulation.

Physical examination revealed a semistuporous, poorly co-operative, woman. There was slight rigidity of the neck. The pupils were equal and reacted well. The knee and ankle jerks were absent, and there was a questionable bilateral positive Babinski reflex.

The blood pressure was 65 systolic.

Examination of the blood revealed a hemoglobin of 11.8 gm. and a white-cell count of 12,600, with 91 per cent polymorphonuclears. The red cells and platelets appeared normal in the smear. The urine was light amber, acid in reaction, had a specific gravity of 1.008, gave a ++ test for albumin and showed a light-green sugar reaction; the sediment contained a rare red cell, 10 white cells and an occasional epithelial cell per high-power field. The nonprotein nitrogen of the serum was 48 mg. per 100 cc., the sugar 141 mg., and the sulfathiazole level 3.1 mg. (she received 15 gm. of sulfathiazole soon after admission). When repeated the next day, the nonprotein nitrogen was 32 mg. per 100 cc.; the bicarbonate was 23.4 milliequiv. per liter. The urine culture demonstrated a nonhemolytic streptococcus. The bleeding time was 2 minutes, and the clotting time 10 minutes. A lumbar puncture revealed an initial pressure of 90 mm. (water). The fluid was clear and contained 1 red cell per cubic millimeter. The total protein was 29 mg. and the sugar 92 mg.

per 100 cc.; the gold-sol curve was normal, and the spinal-fluid Wassermann was negative. An electrocardiogram showed a normal sinus rhythm with a rate of 85; there was evidence of slight left-axis deviation. The T waves were low in Leads 1 and 2, slightly inverted in Lead 3, and very low to biphasic in Lead 4. The urine was negative for follicle-stimulating hormone.

Two days after admission, it was recognized for the first time that the patient had been accustomed to taking thyroid extract and that during her recent illness none had been administered. She was started on $1\frac{1}{2}$ gr. of thyroid daily, and three days later seemed brighter, read the newspaper headlines understandingly and had no complaints. The blood pressure rose to 140 systolic, 90 diastolic. Despite her apparent improvement, eating became a problem for she refused to chew or swallow, although she did not choke on liquids. At times she seemed nauseated. On the sixteenth day her temperature rose to 100°F. and did so during the succeeding days. A urine examination revealed a ++ test for albumin, a specific gravity of 1.005 and negative reactions for sugar and diacetic acid; the sediment was loaded with white cells and amorphous material. When checked several days later, it was acid in reaction, had a specific gravity of 1.020, gave a + test for albumin and contained 2 red cells, 25 white cells and many bacteria per high-power field. The nonprotein nitrogen was 32 mg. per 100 cc., the bicarbonate 18.5 milliequiv. per liter, and the protein 6.7 gm. per 100 cc. Four days later, after being lifted into a chair, the patient immediately became pale, her eyes rolled back, the tongue rolled out of the mouth, and she fell forward and was pulseless. When returned to bed her color came back slowly; the pulse was 132, and the blood pressure 140 systolic, 90 diastolic. That evening the nurse found the patient lying on her back mumbling excitedly and incoherently. She did not respond when called, but when shaken gently she said, "Oh, I have had a nightmare." The next day she seemed mentally clearer but despondent and complained of extreme fatigue. The neurologic examination was negative. The patient died on the following day.

DIFFERENTIAL DIAGNOSIS

DR. MAURICE FREMONT-SMITH: The statement that this patient was very sensitive to mushrooms appears in the history only once.

DR. TRACY B. MALLORY: There was, however, a very clear manifestation of allergy. A soup even slightly flavored with mushrooms would regularly provoke symptoms.

DR. FREMONT-SMITH: But it does not come into the story again.

At the first admission the case is the easiest I have ever discussed. The patient had a stone, and the stone was located. It is worth commenting on two or three things at this point. She was fifty-nine years old and was well. She was taking thyroid; she had pain in the abdomen and red cells in the urine, and they made a diagnosis of renal stone. I want to point out one thing only: that pain in the abdomen and plenty of red cells in the urinary sediment do not necessarily mean stone. An acutely inflamed appendix that lies against the ureter can produce red cells in the urine in good quantity and one cannot therefore rest safely on the belief that there is a stone—it may be caused by the appendix. In this case, it is perfectly clear with the x-ray studies, the flank pain and the removal of the stone that she had a stone! We might think of some calcium upset such as hyperparathyroidism. If bilateral stones? Yes. If staghorn? Yes. If recurring stones? Yes. This stone is described as triangular. I think I am correct in saying that a triangular shape suggests an oxalate stone. We have no evidence for or against any hyperparathyroidism. It is something always to think about in relation to stone. She was discharged from the hospital apparently all right.

After having had a stone removed, the doctors thought she had mild urinary infection and they gave her sulfathiazole by mouth—not a very large amount, and probably not enough to be of significance in her later history.

I shall now discuss the second admission. The patient developed slight fever, probably owing to urinary infection, but she had lethargy, became very weak and tended to sleep most of the time. She also had slight rigidity of the neck. These symptoms are more than you would expect from mild urinary infection, and apparently the suggestion was made that she needed thyroid, which she was given. She improved very rapidly for a very short time, and then died.

I think it would be best to take the one positive finding we have to go on and start from there because it will open up the other lines of approach. "The urine was negative for follicle-stimulating hormone." This is put in in a very innocent way, but it is an important statement. It is absolutely abnormal for a fifty-nine-year-old woman to have a negative follicle-stimulating hormone test. At the menopause the level of the follicle-stimulating hormone goes up. The pituitary gland remains active, and the follicle-stimulating hormone remains elevated to good old age—some people say for the rest of the person's life. Furthermore, it stays up at high levels. When we say it is negative, we mean that the urine contains less than 10 mouse units per 100 cc., and this woman should

have had more than 10, and probably a great deal more than 10, mouse units per 100 cc. of urine.

There are various causes for an absence of follicle-stimulating hormone in a woman past the menopause, and one of these is a destruction of the basophilic cells in the pituitary gland by tumor or possibly by vascular thrombosis. In the first case, we have acromegaly. The tumor of the eosinophilic cells causes destruction of the basophilic cells, and these patients give negative tests for follicle-stimulating hormone. Then there are cases of so-called "panhypopituitarism"; some start at the time of labor following hemorrhage. Thrombosis of the vessels supplying the pituitary gland results, and these patients also have negative follicle-stimulating hormone tests.

I think we can say that panhypopituitarism is out. This woman was always well. She came in apparently a strong, well, woman. Patients with panhypopituitarism are weak, and they rarely live to be fifty-nine. They age very quickly and look very old but most of them die about forty. We have no evidence of acromegaly; there was no headache, and no changes in the visual fields are recorded. I think we can throw out acromegaly.

The other reasons for the absence of follicle-stimulating hormone concern the inhibition of the basophilic cells of the pituitary gland by other endocrines. One is an estrin-producing tumor, which puts the woman back where she was before the menopause. The tumor produces estrin, just as the active ovary gives off estrin, and the pituitary is inhibited and the level of the follicle-stimulating hormone comes down. The same is true of arrhenoblastomas and adrenocortical tumors, the latter producing a masculinizing hormone, which inhibits the pituitary. The arrhenoblastomas, according to Dr. Fuller Albright, produce a substance that inhibits the pituitary gland. Then there can also be lack of follicle-stimulating hormone from protein starvation, the anorexia nervosa group, and disappearance of the activity of the pituitary gland due to myxedema. In the absence of thyroid secretion the pituitary gland does not work properly, and the patient may have a negative test for follicle-stimulating hormone after the menopause.

That brings us to the question of myxedema. Could this woman have had myxedema? Apparently she had been given 8 gr. of thyroid. That may have been Burroughs and Wellcome thyroid, 1 gr. of which is equivalent to $\frac{1}{4}$ gr. of thyroid U.S.P. If so, she would have been getting a dose equivalent to 2 gr. I doubt very much if she could have stood 8 gr. of thyroid if she was myxedematous, although a normal person can stand it. There

are other facts. They gave her thyroid and she improved. Let me go back farther. They did not give thyroid and she went downhill; however, this does not happen that fast in myxedema. It takes a month for thyroxin to disintegrate in the body. A sudden state of thyroid deprivation after stopping thyroid therapy does not develop in twelve days. More than that, they say she was drowsy. She was definitely more than drowsy. She was psychologically inhibited, could not swallow and so forth. Something more than thyroid deprivation had happened to her. We get no help from the spinal-fluid findings. In myxedema the spinal fluid may be identical with that found in brain tumor—high protein and high pressure. Of course in this case the woman had been treated, and a well-treated case of myxedema has a normal spinal fluid. The spinal-fluid protein in myxedema will come down from as high as 242 mg. to 38 mg. after a month of adequate treatment. I do not know about the pressure, but I believe that also returns to normal. Here the spinal fluid does not help to make a diagnosis of myxedema. On the other hand, it does not rule out the diagnosis, because the woman had been treated.

Can we get any help as to the final outcome from the description of the heart situation? The patient is said to have had a big heart with blowing murmurs. Could she have had a coronary thrombosis with emboli in the brain? The electrocardiogram does not bear out a diagnosis of coronary thrombosis. She undoubtedly had coronary disease, but I do not believe that one can make a diagnosis of coronary thrombosis on that electrocardiogram.

I should be grateful to know if the patient had had a tooth out just before she came in. If so, I can make a very hypothetical picture that may be correct. If she had a tooth out she might very well have had a nonhemolytic streptococcus infection of the kidney, something that frequently follows tooth extraction.

DR. WILLIAM B. ROBBINS: She had had no tooth out.

DR. FREMONT-SMITH: All right, I was just going to say that she might have had subacute bacterial endocarditis on the same basis, with infarcts in the brain and other parts of the body. I do believe that this woman had an intracranial accident, and I am not satisfied to explain her symptoms and death on the basis of myxedema, which she may well have had. I believe she had an intracranial accident, and the most likely, on the basis of statistics, is thrombosis of a cerebral vessel. I shall leave that as my diagnosis, plus the question of myxedema.

DR MALLORY Have you anything to show that will help, Dr Holmes?

DR GEORGE W HOLMES The kidneys are normal in size and shape. Then I should like to point out these large gas filled loops of bowel. When a patient has stones there is an unusual amount of gas in the small bowel. Here is a beautiful demonstration of the stone picked up by the urologist's instrument.

DR JAMES B AYER The neurologic examinations, except the first one when she came in the second time, were always negative. The mental picture was one predominantly of lethargy. She was never in complete coma, but was lethargic. She fell asleep while talking, but on waking up she was quite well, never irrational. On one occasion she showed exceptional memory for recent and past events.

DR JURGEN RUESCH A prolonged disturbance of consciousness usually indicates a cerebral lesion, whereas lethargy may point to an involvement of the hypothalamus and the basal ganglia.

The fluctuating blood pressure may also indicate a lesion around the centers of the medulla oblongata. Confusion is not inconsistent with lesions in the upper cervical spine and the oblongata.

The possible cerebral lesion might have been produced by the three sulfonamides, which were given in rapid succession. In the literature, a number of cases have been described in which psychosis, disturbances of consciousness and confusion developed after use of these drugs. The majority of these patients recovered, a few, however, died. The pathology found consisted either of areas of softening or of multiple punctate hemorrhages.

In the present case I should expect a diffuse lesion in the brain.

DR STANLEY COBB I think perhaps we overlook the effect of the sulfonamides on the individual psychologically. Almost always there is some effect,—always a little confusion,—and I wonder if this is not a person especially susceptible to them. I believe we should be on the lookout for that effect and a bit more afraid of it than we are.

DR GEORGE G SMITH The thing that struck me about this patient was the peculiar type of lethargy. As Dr Ayer has said, she was not depressed when she woke up and not confused. She smiled and said just a few words and immediately went to sleep again. Along with that there was a marked depression in the blood pressure, which was around 60 systolic for a few days, as I remember it. The pus in the urine later on I think was accounted for by the fact that she was on constant drainage because she did not void. I expected that the mental condition would clear up immediately when we stopped the sulfonazole. I believed at

first that she might have had a cerebrospinal meningitis, because she had had spinal anesthesia. A lumbar puncture showed no evidence of that. I soon realized that she was entirely beyond my crude methods of diagnosis and called in the neurologic experts.

CLINICAL DIAGNOSIS

Hypothyroidism?
Acute myocarditis?

DR FREMONT-SMITH'S DIAGNOSES

Cerebral thrombosis
Myxedema?

ANATOMICAL DIAGNOSES

Sulfonamide nephrosis
Hypertrophy of heart, slight
Aberrant thyroid tissue
Hurthle cell adenoma of aberrant thyroid
Encephalitis, toxic, slight.

PATHOLOGICAL DISCUSSION

DR MALLORY The anatomical findings in this case were very interesting, but I think they leave open the question whether they explain the clinical state and the demise. An outstanding finding at autopsy was in the kidneys. Dr Holmes has demonstrated that, in the film taken during the first entry when the patient had a stone, the size of both kidneys was perfectly normal. At the time of autopsy they were twice normal size, weighing over 500 gm., and were extremely swollen and very pale. On microscopic examination they showed a picture that we have begun to associate with reaction to the sulfonamide drugs. Our resident pathologist, Dr Maisel, working at Cornell last year in collaboration with Drs McSwain and Glenn,* studied the effects of prolonged administration of sulfonamide drugs in dogs. They have described an apparently specific lesion of the renal parenchyma, which is entirely independent of the precipitation of crystals in the tubules and pelvis. I am going to read Dr Maisel's description of the renal picture in this case, and then ask him to compare it with the experimental findings.

The sections of both kidneys are similar in appearance. No abnormality is recognized in the glomerular tufts. However, Bowman's space and the tubular system contain a hyaline glassy-blue protein material. Many of the tubular lining cells particularly in the cortex, are poorly stained, the cell outlines are indistinguishable, and the nuclei are often pyknotic or absent. In many areas there is a break in the continuity of the tubular lining epithelium and basement membrane. Here the hyaline protein casts have been ex-

*Maisel B, McSwain B, and Glenn F. Lesions produced by sulfonamides. *Proc Soc Exper Biol & Med* 49:715-717, 1942.

truded into the stroma. Inflammation is present in the stroma, frequently concentrated about the extruded protein casts, consisting of monocytes, epithelioid cells, multinucleated giant cells, a few lymphocytes and polymorphonuclears and a small number of plasma cells. Fibroblasts are present in some of these areas. A few of the collecting tubules contain many polymorphonuclears. No bacteria are recognized in sections stained by the Gram and Giemsa methods. About and in the walls of several veins, especially those of the peripelvic group, there are patchy areas of inflammation consisting of plasma cells, lymphocytes and a moderate number of polymorphonuclears. Mural thrombi are attached to the walls of veins overlying these foci of inflammation, and a few veins are completely thrombosed. The arteries appear normal.

DR. BERNARD MAISEL: It seems to me that there are several interesting things to learn from this case. This woman received relatively small doses of three different sulfonamides, thus making it difficult to incriminate any one. However, one is justified in saying that she reacted unfavorably to the sulfonamide group. This was manifest primarily in the psychobiology and in the kidneys. The mental picture has been discussed as fully as we are able to at present. As for the kidney changes, she developed albuminuria; and blood elements and transitional epithelial cells appeared in the urine. At no time were crystals of sulfonamide noted. Thus, renal injury developed without the presence of sulfonamide crystals and persisted several weeks after the drug administration was stopped. The nonprotein nitrogen did not exceed 48 mg. per 100 cc. and was usually lower than this. This does not point to glomerular damage, yet some change in glomerular filtration must have occurred, since protein and blood elements escaped to the urine.

Histologically, the changes resemble those noted in our animal studies. In the dogs, the tubules, particularly the proximal and distal convoluted tubules, were swollen and the lining cells were often necrotic. The lumens were filled with cellular debris and metachromatic, often glassy-blue, hyaline material, which we believe to be characteristic of a protein-sulfonamide combination. In some areas this material escaped from the tubules into the stroma. Here a granulomatous inflammation developed, and after approximately two and a half to three weeks, which coincides with the time interval in this case, multinucleated giant cells developed. The glomeruli in this case did not appear abnormal except for the blood elements in Bowman's space. However, in several of the experimental animals some were destroyed. In the dogs there was often an elevation of the urea nitrogen of the blood above 100 mg. per 100 cc., and a few developed blood-pressure elevations. In these animals it was interesting that, as the urea nitrogen

rose, the sulfonamide level rose, suggesting drug retention by damaged kidneys. Another interesting change in the kidneys of this case was the presence of inflammation about and in the walls of the veins, many of which were thrombosed. Often the thrombus was attached in an area of inflammation. The arteries in this case were normal, but our previous studies showed that an arteritis may occur. Finally, the bone marrow obtained from the lumbar vertebral bodies was moderately depressed, a condition that can be experimentally produced in the dog.

This case represents the first example in a human being that we have seen or heard of showing extensive granulomatous inflammation of the kidney as a result of the sulfonamide therapy. The injury obviously did not follow obstruction of the tubules by sulfonamide crystals.

DR. MALLORY: Dr. Maisel has permitted me to study many of his animal slides, and I agree entirely with him that the changes in this patient's kidneys are identical in type. Following his pointing out of the lesion to us, we have seen numerous kidneys with minor changes of this nature in patients who had received sulfonamides, but never anything approaching this grade of severity. It is of great interest that the total dosage was not great and that the levels which were attained in the blood stream were never particularly high. Possibly in that respect the history of allergy to mushrooms is important. She was an allergic person and may have had a hypersensitive response to comparatively small amounts of drugs.

Another interesting finding was a tumor behind the esophagus, which on microscopic examination caused us considerable trouble, because we could not decide at first whether it was a bit of aberrant thyroid tissue that had undergone degeneration into a fetal adenoma or whether it was a parathyroid adenoma. It was composed entirely of bright-red cells, so, if it was parathyroid tissue, it would have been the oxyphilous type and probably nonfunctioning. I think it is more probable, since we found a second nodule that was definitely an ectopic thyroid gland, that this first nodule was also of thyroid origin and represented a Hürthle-cell adenoma. That is merely an academic issue, however.

The brain showed nothing grossly. Dr. Kubik has been over it carefully microscopically. It is not normal, but that is about all he is willing to say about it. There is a slight but rather diffuse reaction in the cortex shown mostly by slight swelling and slight increase in the number of the microglial cells in the white matter. That is the only point on which he would definitely commit himself. He has seen somewhat similar pictures in cases with

uremia, and a variety of other disease states. It is the brain of a sick person, and that is about all one can say about it.

DR. ROBBINS: According to the time interval, the evidence of uremia was slight. It did not seem like uremia.

DR. MALLORY: The highest recorded nonprotein nitrogen was 48 mg., and it sank after that. It is hard to make out a picture of uremia and yet the kidneys were the major anatomical finding.

DR. FREMONT-SMITH: Was there anything in the thyroid to indicate myxedema?

DR. MALLORY: It seemed a little on the atrophic side. I cannot possibly make a diagnosis of myxedema from it. The pituitary gland was normal.

DR. ROBBINS: The thyroid was Burroughs and Wellcome, and after she was in the hospital she was given Armour's.

DR. OLIVER COPE: Three grains of thyroid a day ought to cause atrophy of the thyroid gland, atrophy of disuse. Dr. Mallory's description might well be accounted for on the basis of taking thyroid over a long period rather than true primary atrophy. I might also say that 90 per cent of the renal calculi occurring in hyperparathyroidism are unilateral. This condition should be excluded in any case of renal lithiasis.

DR. FULLER ALBRIGHT: I have seen several elderly patients with panhypopituitarism.

DR. FREMONT-SMITH: Was there any explanation of the negative test for follicle-stimulating hormone?

DR. MALLORY: Not unless she had myxedema. There was no tumor of the ovaries or adrenal glands.

DR. ROBBINS: I think she was always myxedematous. I had known the patient for years, and she was the myxedematous type—fat and heavy, with red cheeks.

DR. MALLORY: Since we have quite good proof of a severe sulfonamide reaction in one organ, it is not unreasonable to guess that the cerebral pathology might also be on the same basis. I do not believe we can go farther.

CASE 28502

PRESENTATION OF CASE

First admission. A fifty-seven-year-old man was admitted because of dyspnea, palpitation and loss of weight.

About three months prior to admission he began to suffer with exertional dyspnea, palpitation, evening ankle swelling and loss of weight and strength. His appetite increased; he was said to have become nervous and irritable and his eyes became more prominent. His voice seemed to have become somewhat hoarse.

Physical examination revealed a thin, nervous man with a moderate bilateral exophthalmos, and an obvious tremor of the hands. The thyroid gland was symmetrically enlarged. The heart was found to be enlarged, and the sounds were irregular in time and quality. A systolic murmur was audible at the apex. The neck veins were distended. The blood pressure was 135 systolic, 75 diastolic, and the cardiac rate was 120.

An x-ray film of the chest showed that the heart was considerably above normal in size. The greatest prominence of the heart shadow was in the region of the right auricle. There was no unusual prominence of the pulmonary conus or left auricle. There was a moderate tortuosity of the aorta. The lung fields were clear. The basal metabolic rate was repeatedly above +35 per cent. An electrocardiogram showed auricular fibrillation, with a rate of 110; the T waves were rather low in all leads.

After a course of Lugol's solution and rest the basal metabolic rate was +16 per cent. During hospitalization he received 3 gr. of quinidine daily, which slowed his cardiac rate slightly and produced a more regular rhythm. A bilateral subtotal thyroidectomy was done, and the removed glandular tissue showed hyperplasia. Following this his symptoms were markedly improved and he gained weight. He was discharged from the hospital on a daily dose of 10 drops of Lugol's solution and 3 grains of quinidine sulfate per day.

Second admission (two and a half years later). The patient was readmitted because of a moderate amount of dyspnea, palpitation on exertion and dull nonradiating precordial pain that had developed during the preceding eleven months. Several months previously on his own volition he had ceased taking the Lugol's solution and the quinidine sulfate.

Physical examination revealed essentially the same findings as noted in the previous admission except that only a nodule of thyroid tissue was felt in the right side of the neck at the clavicle. The blood pressure was 115 systolic, 75 diastolic. The basal metabolic rate was +40 per cent. An x-ray film of the chest revealed that the heart had increased only slightly since the previous examination.

He was again treated with Lugol's solution, and later digitalis was administered. Under local anesthesia the thyroid nodule was excised; histologically it resembled the previously removed thyroid tissue. After the operation, because of a persistent auricular fibrillation, the digitalis treatment was stopped and quinidine sulfate substituted, with a marked improvement in the cardiac rate, and

rhythm. He was discharged from the hospital on the same drug routine as previously advised after the initial operation.

Final admission (ten years later, at the age of sixty-nine). Eleven months after discharge he noticed several brief attacks of substernal pressure, particularly after walking rapidly, and "spells" of palpitation. Physical examination in the Out Patient Department revealed only distant heart sounds and a rumbling systolic murmur maximum in the region of the xiphoid process. The cardiac rate was slow, and the rhythm regular. The blood pressure was 110 systolic, 62 diastolic, and the pulse rate was 72. The basal metabolic rate was -18 per cent. The symptoms continued without appreciable change in degree, and a physical examination a year later was remarkable only because a loud systolic murmur was then heard in the aortic area. No thrill was felt, and no diastolic murmur was audible. Six months later the murmur was described as hard and grinding, being audible over the entire precordium and replacing the first heart sound. The patient was able to engage in heavy work as a longshoreman despite the continuance of attacks of dyspnea and substernal pressure. Eight months prior to admission he noticed a progressively increased limitation of activity because of dyspnea and tightness across the chest. Both these symptoms disappeared after a few minutes of rest. On the day of admission, while at his usual work as a longshoreman, he felt a tightness in the chest. Sudden air hunger developed, and he collapsed.

Physical examination revealed an ashen pale man sweating profusely, sitting upright in bed and having extreme respiratory distress. He inhaled rapidly, and expirations were prolonged and labored. He was obviously quite restless. He could not speak, and responded only with grunts. The heart was somewhat enlarged to percussion. The heart sounds were of good quality. The cardiac rhythm was very irregular. A loud harsh systolic murmur was audible at the apex and transmitted with greatly diminished intensity to the left axilla. There was a soft blowing systolic murmur in the aortic area. Rales were prominent in both lungs. The abdomen was soft. The liver edge was felt about one fingerbreadth below the costal margin. There was no peripheral edema.

The blood pressure was 110 systolic, 60 diastolic. The temperature was 100.4°F ., the pulse 95, and the respirations 29.

The examination of the blood revealed a hemoglobin of 15.5 gm., a red-cell count of 5,300,000 and a white-cell count of 28,000, with 71 per cent polymorphonuclears. An electrocardiogram showed a regular cardiac rate of 140. The PR interval was

0.19 to 0.20 second; the QRS complex was notched; T_1 was inverted, with a low take-off of the ST segment in this lead, and T_2 was diphasic.

An electrocardiogram taken several hours later revealed a regular cardiac rate of 110. The PR interval was 0.20 second. The QRS complex was 0.10 second and was notched in Lead 2; T_1 and T_2 were diphasic; and there was evidence of a moderate left-axis deviation.

Despite the repeated administration of morphine, aminophyllin and oxygen and attempted, partially successful, phlebotomy, the patient became increasingly dyspneic and cyanotic and expired twelve hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE: This case had a dramatic denouement that I learned about after the patient's death but which I did not guess during his life, and would not, I am sure, have thought of now. I shall tell you the reasoning I went through on the one occasion that I saw the patient in consultation. I do not remember the details of the post-mortem findings; I simply recall one important point, which was very surprising.

The heart was enlarged, the sounds irregular in time and quality, suggesting auricular fibrillation. There was a systolic murmur at the apex, and the neck veins were distended. We are led to wonder if this was a so-called "thyrotoxic heart" or merely a temporary effect of thyrotoxicosis on the heart or whether the thyrotoxicosis was superimposed on organic heart disease. Enlargement of the heart and distention of neck veins mean heart failure. There are likely to be other causes for this than thyrotoxicosis alone.

Frequently there is an increased pulmonary-conus shadow in thyrotoxicosis. The electrocardiographic finding of auricular fibrillation confirms the suspicion of that arrhythmia on physical examination; the statement about the T waves is unusual, for low T waves are characteristic of thyrotoxicosis. At one time we thought that since the T waves were flat in myxedema they should be high in thyrotoxicosis. Years ago Dr. Joseph Aub and I reported that there was no characteristic T wave in thyrotoxicosis; it tends to be low rather than high. Since then we have learned that high sympathetic tone depresses the T waves and that high vagus tone elevates them.

"During hospitalization he received 3 gr. of quinidine daily, which slowed his cardiac rate slightly and produced a more regular rhythm." That is not specific enough to point to the effect of the quinidine. Then there are remarks about less fibrillation. Fibrillation is a condition that is there or is not there. There may be a variation

in heart rate in fibrillation that is responsible for inaccurate reference to the degree of fibrillation. What one wants to know is whether there was persistence of fibrillation or a return to normal rhythm. This statement about a more regular rhythm is not good enough. Was there a return to normal rhythm? Was there a later electrocardiogram? There is no statement that the rhythm had returned to normal after the second admission.

The patient's condition at the time of his second admission suggests several different things. He may have had effort syndrome (neurocirculatory asthenia), which would give precordial oppression, dyspnea and palpitation. Angina pectoris would not ordinarily cause palpitation. Paroxysmal fibrillation usually does not occur at the same time as angina pectoris, they are two independent symptoms.

"... and a rumbling systolic murmur maximal in the region of the xiphoid process." That is an odd description. I do not know that I have ever heard a rumbling systolic murmur. It sounds as if it must have been a rough murmur or a grating murmur or mixed up with diastolic murmurs. Diastolic murmurs can certainly be rumbling but I do not think a systolic murmur can be. It was heard at the xiphoid process, low down. It is a little hard to decide about that at the present moment.

Then we have a statement that the rhythm was regular, years after paroxysmal fibrillation. Arrhythmias due to thyrotoxicosis can be controlled by thyroidectomy alone, or with the help of quinine and iodine. I should like to ask Dr Lerman about the frequency of recurrence of thyrotoxicosis after thyroidectomy.

DR. TRACY B. MALLORY: There is a definite statement that when he came in at the time of the second admission he was fibrillating. When he left the hospital at that entry the rhythm was regular.

DR. WHITE: That is according to Hoyle.

"A loud systolic murmur was then heard in the aortic area." There is no statement about the murmur that had been heard at the xiphoid process. I dare say that this is the same murmur that was described before as rumbling and heard at the lower end of the sternum. I expect that it had also been heard in the aortic area previously but not so specified. The "grinding" murmur heard over the entire precordium makes one think, of course, of an aortic stenosis murmur. Such a murmur varies a good deal in intensity according to the condition of the patient and tends to be very widespread over the precordium, more widely spread over the precordium than any other murmur. An aortic stenosis murmur is not heard so

well in the lung bases as elsewhere, for example, at the apex and lower end of the sternum. I suspect that this was the same murmur as that heard ten or twelve years previously. Underlying his condition the patient probably had an old aortic stenosis, which became more evident with increasing years. A calcareous aortic stenosis is likely, superimposed on some underlying aortic-valve disease. It is not necessary to diagnose an underlying rheumatic aortic valve lesion, but at any rate it is probable that he had had aortic stenosis for a long time. I have seen patients with aortic stenosis able to work very hard for many years when middle aged or older until rather abrupt heart failure set in, after which they did poorly. It says "heavy work as a longshoreman." He must have been a strong man.

He then showed both coronary and myocardial insufficiency. That may happen in the same person, but usually it is one or the other; either the myocardium fails or the coronary circulation fails, but one can have both fail almost simultaneously. Whether that took place prior to the final attack that brought him to the hospital, I am not sure, but while at work he had felt a "tightness across the chest."

There then occurred a sudden serious cardiovascular accident of some sort, not necessarily in the heart, and with it, apparently, left ventricular failure. What kind of accident could it have been? That is the problem we must try to decide.

We now have a different description of the physical examination than that previously given. He was desperately ill with a change in murmurs. There was no peripheral edema, no suggestion of right heart failure. The dyspnea increased. Possibly he had a pulmonary accident, of which I shall speak in a moment.

This change in murmurs is interesting. That often happens. Sometimes we have been confused or unable to diagnose aortic stenosis in these exercises because the patient was too sick to allow the hearing of the characteristic aortic stenosis murmur, which undoubtedly would have been heard, is in this case, when the patient was relatively well. The apical murmur evidently had increased. It is not likely that the aortic systolic murmur suddenly became louder at the apex as it failed at the base. It was more likely the result of some change elsewhere, most easily explained by the development of left ventricular dilatation, with superimposed mitral regurgitation. He did not have a high degree of shock so far as the blood pressure is concerned. The high white-cell count is somewhat against the first diagnosis that I should think of, namely, myocardial infarction. The electro-

cardiogram showed a regular cardiac rate of 140. We are not told whether the heart rhythm was normal. The record suggests that it may have been. At first the pulse rate had been 95, but by the time the electrocardiogram was taken the rate was 140. It might have been an abnormal rhythm but regular (for example, auricular flutter). However, the description is that of normal rhythm. "... T₁ was inverted, with a low take-off of the S-T segment in this lead. . . ." That often happens to T₁ or ST₁. One has to pay more attention to Leads 1 and 4 than to the other leads. The rhythm apparently remained regular. The electrocardiogram is not specific, although confirmatory, of coronary insufficiency, dependent usually on coronary heart disease but now and then also encountered in stenosis when there is a large heart and inadequate coronary circulation without actual myocardial infarction or even much of any coronary narrowing.

I should say that this patient died in left ventricular failure possibly due to coronary insufficiency. The underlying trouble I can state definitely was an old cured thyrotoxicosis, doubtless also calcific aortic stenosis, and quite likely coronary heart disease. We have no proof that patients with aortic stenosis can have this picture without coronary disease or coronary occlusion, but it is possible at seventy-one. Then the final fatal illness is interesting. There was no pain associated with this. There is a choice of several things, but there is about an even bet between painless myocardial infarction preceding heart failure and massive pulmonary embolism. In one way pulmonary embolism would explain the absence of pain and the marked dyspnea better than would myocardial infarction. I have seen painless myocardial infarction complicate a condition such as this in a patient with earlier angina pectoris. A less likely possibility is painless dissecting aortic aneurysm with heart failure. A rupture of the aorta of any other type and rupture of the aorta into the pulmonary artery would give different physical signs, the latter producing a continuous murmur like that of patency of the ductus arteriosus. That is not likely here but should be mentioned as a remote possibility. Pulmonary thrombosis or thrombosis elsewhere than in the heart or lungs, that is, cerebral or peripheral, is undiagnosable in the absence of any localizing evidence. Was there cardiac tamponade from hemopericardium due to rupture of heart and aorta? Probably not, since the blood pressure was too good and the veins were not engorged.

A PHYSICIAN: Is it possible that there was a rupture of one of the aortic cusps from calcareous stenosis?

DR. MALLORY: I do not believe we have ever seen that.

DR. JACOB LERMAN: I should like to comment on the initial onset of the disease. When I first saw the patient he had relatively recent onset of hyperthyroidism, and in the presence of a large heart and fibrillation we assumed that he had independent heart disease. Further studies verified the fact that he had coronary heart disease, and he eventually developed aortic stenosis.

Dr. White asked about recurrent thyrotoxicosis. The average incidence varies from 10 to 20 per cent following subtotal thyroidectomy, the smaller figure being in the group with more radical surgery and the larger in those with less radical surgery. This patient had recurrences; the first was removed, but he had another after the second operation. Fortunately that burned itself out and became normal after a long period of iodization.

DR. WHITE: Would the figure be as high as 20 per cent for recurrent thyrotoxicosis severe enough to require a second operation?

DR. LERMAN: Yes, if those cases controlled by iodine and rest are not included; of the latter, only about 5 per cent come back for operation.

DR. WHITE: One other point: the appearance of auricular fibrillation with each episode of thyrotoxicosis and its disappearance with relief of the toxic state is a very common finding. The auricular fibrillation may disappear even before operation through iodine alone and certainly post-operative four or five days after the temperature is normal. Many times it is recurrent when thyrotoxicosis makes itself manifest. It may or may not come back again after recovery.

CLINICAL DIAGNOSES

Arteriosclerotic heart disease.
Calcareous aortic stenosis?
Calcified annulus fibrosus?
Left ventricular failure, acute.
Pulmonary edema.
Coronary occlusion?

DR. WHITE'S DIAGNOSES

Recurrent thyrotoxicosis and auricular fibrillation (in past).
Aortic stenosis, marked.
Acute congestive heart failure, secondary to acute myocardial infarction, pulmonary embolism or some other factor.

ANATOMICAL DIAGNOSES

Calcareous aortic stenosis.
Calcification of mitral valve and chordae tendinae, with stenosis.
Rupture of mitral chordae tendinae, with terminal mitral insufficiency.
Hydrothorax.

Bronchopneumonia, slight, terminal.
Chronic pancreatitis, with fat necrosis.
Operative scar: thyroidectomy.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The post-mortem examination showed that this man did have severe valvular heart disease as Dr. White predicted. There was a long-standing calcareous aortic stenosis a little unusual in character. All the valve cusps were thickened, and on the sinus side of each cusp was a warty excrescence, each of which was densely calcified. The calcification extended up to the very margin. There was no interadherence at any of the commissures. It is very characteristic of rheumatic heart disease that the aortic cusps should become interadherent. So this absence of interadherence is a point against a rheumatic etiology. Many cases of aortic stenosis of this type show absolutely normal mitral valves. However, in this case the mitral valve was not normal. It, too, showed a moderate degree of stenosis. The circumference measured 6.5 cm, as compared with the normal of 10 cm. It was likewise extensively calcified. It was not quite the ordinary picture of rheumatic mitral stenosis, however, in that the leaflets were not interadherent and the calcification was more marked in the annulus than in the cusps themselves. The chordae tendineae attached to the mitral valve were likewise calcified, and the final sudden dramatic episode was quite clearly the result of sudden rupture of many of these chords attached to the posterior flap of the mitral valve. Half a dozen of the chords had broken sharply across so that the leaflet of the valve was without anchorage and was flapping loosely, at least in so far as its degree of calcification would permit. So there must have been a sudden and dramatic mitral insufficiency, which accounted for the terminal episode. There were no scars in the

myocardium. The coronary arteries were large and capacious; there was an occasional atheromatous plaque but nothing that appeared to narrow the lumens. Throughout the rest of the aorta the patient had far less arteriosclerosis than the average man of his age. It looked like the aorta of a patient of forty-five and he was seventy.

DR. WHITE: What did you find in the aorta? Was there any relation between the aortic-valve calcification and the sclerosis of the aorta itself?

DR. MALLORY: By and large, patients with calcareous aortic stenosis show less atheroma than other persons of their age. That is quite regularly true in the ascending aorta. In this case it was also true in the descending and abdominal portions. We have numerous sections of the myocardium. I can see nothing that to my eye constitutes conclusive evidence of rheumatic infection. I think in this case one has to leave the question of etiology open.

DR. WHITE: A very important point is that the abnormality of the electrocardiogram was due not to coronary heart disease but to aortic stenosis.

A PHYSICIAN: Have you made any observations relative to the degree of coronary sclerosis in these patients who have had hyperthyroidism? It has been my feeling that they seem to preserve their youth.

DR. MALLORY: I have not seen enough cases to have any strong personal opinion about it. There is a good deal in the literature, both clinical and experimental, to suggest that hyperthyroidism tends to retard the deposit of atheromatous material, whereas myxedema tends quite uniformly to increase it.

DR. WHITE: What Dr. Mallory has just said is about in accord with my experience. Certainly, arteriosclerosis is common with myxedema but I doubt if it is in thyrotoxic cases, since relatively few of them have angina pectoris.

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THE SIGNIFICANCE OF THE RH FACTOR

Blood transfusion is usually a dramatically beneficial procedure. If it is accompanied or followed by a hemolytic reaction, however, it may be distressing both to the patient and to the physician. The commonly employed precaution of giving matched blood, usually of the homologous group, has made such reactions the exception rather than the rule. But even in intragroup transfusions, when cross matching has shown apparent compatibility, occasional reactions have occurred without apparent reason. One of the commonest causes for such reactions has now been disclosed by the work of Levine¹ and Wiener,² each of whom

demonstrated that red blood cells containing the so-called "Rh factor" (Rh+), present in 85 per cent of the white population, may be agglutinated by an anti-Rh agglutinin in the blood of a person lacking this factor in his red cells (Rh-). This agglutination results in a hemolytic reaction.

All physicians should be, and probably most of them are, aware of the following important facts, which were pointed out in a paper by Dr. L. K. Diamond on "Hemolytic Transfusion Reactions Due to the Rh Factor" in last week's issue of the *Journal*:

Rh- persons (those lacking the Rh factor in the red cells) may develop an agglutinin against the Rh factor by one or more transfusions of Rh+ blood. Subsequent transfusions of such blood may lead to serious hemolytic reactions.

Rh- women married to Rh+ men may develop this anti-Rh agglutinin during the gestation of an R+ fetus, since this blood factor is inherited as a dominant characteristic from the father. In such cases even the first transfusion with Rh+ blood may produce a serious, if not fatal, reaction. Such a transfusion tends to be common since, too often, the husband is used as the donor for the wife who requires blood. In addition, Levine³ has shown that an Rh+ fetus may be affected by the mother's anti-Rh agglutinin and develop all the signs of the serious intrauterine hemolytic disturbance commonly known as erythroblastosis foetalis.

Rh- women of child-bearing age given transfusions of Rh+ blood may be stimulated to the development of anti-Rh agglutinins that will produce erythroblastosis foetalis in infants of subsequent pregnancies.

The present-day increase in the number of blood banks has led to an increase in the number of transfusions administered. Theoretically, of every 1000 transfusions, 150 are given to Rh- recipients, and 85 per cent of them, or about 128, ordinarily receive Rh+ blood. This may stimulate the development of an antibody against the Rh factor, and after a relatively short interval another transfusion with Rh+ blood given to the same recipient is likely to cause a harmful reaction. In war injuries and in accident cases, multiple transfusions are often necessary, and the danger of transfusion reactions in Rh- recipients is greatly increased.

It therefore becomes imperative that Rh typing of blood be carried out, possibly on every member of the armed forces, and certainly on all patients requiring multiple transfusions or having had a previous transfusion, and on women of child-bearing age or those who have had infants with erythroblastosis foetalis. For the Rh- patient it has been shown repeatedly that only Rh- blood can be used with safety. It is commendable that in Boston an organization—the Blood Grouping Laboratory—has been formed by the Boston Lying-in Hospital, the Massachusetts Memorial Hospitals and the Children's Hospital for the express purpose of assisting other hospitals and individual physicians in properly handling cases of this type.

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CHRISTMAS SEAL CAMPAIGN

THE war against tuberculosis, like the war against Hitler, finds the American people with victories won, but final victory yet to win. This is an enemy that never grants an armistice, and will never receive one. The Annual Christmas Seal Campaign of the National Tuberculosis Association, coming this year when we are deep in war, reminds us of a vital sector of the battle against disease.

Largely through the funds contributed in past years, the death rate from tuberculosis has been cut by 80 per cent since 1900. Since the last war, the development of x-ray examinations on a wide scale has aided materially in the discovery and early treatment of incipient tuberculosis. Special sanatoriums have been multiplied, and diagnostic clinics have been placed within the reach of all. Yet no drug has been found to cure the disease. It still causes more deaths in the age range of fifteen to forty than any other disease, being second only to accidents in the fatalities it brings, and the number of deaths at all ages is four or five times as great as the total of all other acute com-

municable diseases, except pneumonia and influenza.

In wartime, as is well known, the incidence of tuberculosis always increases: war adds to its forces the battalions of poor diet, lowered resistance and congestion of populations, all of which are predisposing to the disease. These evils are as yet largely confined to foreign countries, and preliminary figures for 1942 indicate that tuberculosis deaths in the United States will be the lowest on record. On the other hand, the American people have not so far been subjected to actual wartime conditions. The full impact of war on the campaign to control this disease will probably be felt during the coming year. This being so, those who purchase Christmas Seals will in a large sense be contributing to the national defense.

The campaign total has been set at \$8,000,000. Of the funds received, only 5 per cent will go to the National Tuberculosis Association for the maintenance of its headquarters and other running expenses; the rest will be allocated to states, counties and local communities. It will be used to carry on preventive work, to provide x-ray equipment and other diagnostic facilities and for kindred purposes. Special appeal is being made, as usual, for one-dollar and two-dollar contributions, which are within the reach of nearly all.

The American public has never failed to respond to appeals that arise from crises and threats of danger. To have a part, no matter how small, in the Christmas Seal Campaign is a privilege that millions will embrace, and that no one can in good conscience ignore.

OBITUARY

EDWIN EVERETT JACK

1863-1942

DR. EDWIN E. JACK, eminent ophthalmologist, was a Bostonian of the Bostonians by both birth and education. Entering from the Boston Latin School, he graduated from Harvard College and from the Harvard Medical School. In 1916, he was married to

Groom Denny, whose family roots in Boston were as deep as his own. This marriage was complementary to an unusual degree.

Early in his medical career he specialized in ophthalmology, and after serving for two years as house officer at the Massachusetts Eye and Ear Infirmary he became ophthalmologist to St. Elizabeth's Hospital and the Boston Dispensary; he was a member of the staffs of the Boston City Hospital, the Children's Hospital and the Eye and Ear Infirmary, of which institution he was made a consultant in 1926.

He was a member of The Country Club, the Harvard Club of Boston, the Thursday Evening Club of Brookline, the Massachusetts Medical Society, the American Medical Association, the New England Ophthalmological Society, of which he was past president, and the American Ophthalmological Society.

He never encumbered medical literature. His articles represented valuable and original contributions to his specialty. He owed his large practice not only to his knowledge and his operative skill but also to his gentleness and kindness to "all sorts and conditions of men" and women. These qualities won for him a high place in the family of "Beloved Physicians." Edwin Jack possessed and acquired many other admirable qualities that endeared him greatly to his colleagues and to his friends. He was a lover of the open spaces and traveled extensively. For many years he and his wife rarely missed a Boston Symphony Concert, and during the later years of his life, one of his chief joys was listening to fine music over the radio. He became a most appreciative and most reliable musical critic.

Someone has said, "The more I see of dogs, the less I think of men." Edwin Jack might well have made this remark, for his love of gentle and knowing canine friends was deep and was quickly reciprocated. Hidden by his gentleness were also the finest qualities of the soldier. After his retirement from practice he was obliged to face a series of serious illnesses, several of which involved painful operations and prolonged convalescence. He not only met them with complete bravery but achieved an optimism that approached gaiety. For several years he had known of the existence of the serious heart affliction that finally gave him release. He bore it placidly, mastering its discomforts, retaining his joy in life and in companionship and facing the future without dismay. "For unto every one that hath shall be given," and he was given the promised "abundance." If I read his life rightly, I realize that he gave in turn to medicine an Ideal of Conduct. To those of us who knew

him and loved him, he confirmed the saying of Ecclesiasticus, "A faithful friend is a strong defense . . . and is the medicine of life."

R. B. O.

MEDICAL EPONYM

SIMS'S POSITION

The position which James Marion Sims (1813-1883) described is not that which generally goes by his name at the present time, as will be seen from the following description, which appears in his article "On the Treatment of Vesico-Vaginal Fistula" in the *American Journal of the Medical Sciences* (N. S. 23:59-82, 1852). (By a curious misprint, although the pages from 1 to 60 are consecutively numbered, the page which should be 61 is 51, and the remaining pages of the volume are numbered consecutively from this point so that there are two series of pages numbered 51 to 60. The page reference of the following quotation should really be 69-92.)

In order to obtain a correct view of the vagina canal, I place the patient upon a table about 2½ feet, on her knees, with the nates elevated, and the head and shoulders depressed. The knees must be separated some 6 or 8 inches, the thighs at about right angles with the table, and the clothing all thoroughly loosened, so that there shall be no compression of the abdominal parietes. An assistant on each side lays a hand in the fold between the glutei muscles and the thigh, the ends of the fingers extending quite to the labia majora; then, by simultaneously pulling the nate upwards and outwards, the os externum opens, the pelvic and abdominal viscera all gravitate towards the epigastric region, the atmosphere enters the vagina, and there, pressing with a weight of 14 lbs. upon the square inch, soon stretches this canal out to its utmost limits, affording an easy view of the os tincae, fistula, &c. To facilitate the exhibition of the parts, the assistant on the right side of the patient introduces into the vagina the lever speculum. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

RESOLUTIONS ON THE DEATH OF ALLEN GREENWOOD

WHEREAS, The death of Allen Greenwood, consultant in ophthalmology, has terminated an unusually long and continuous service to the Boston City Hospital (appointed ophthalmic and aural intern in 1889) with great distinction; and

WHEREAS, His passing has deprived us of a skillful and experienced teacher and consultant whose sympathetic understanding and generosity brought relief to so many; and

WHEREAS, His unselfish devotion to his professional duties will never be forgotten by his patients, nor his loyalty by his associates; be it therefore

RESOLVED, That we, the Senior Staff of the Boston City Hospital, express to the family of Allen Greenwood our sincere sympathy; and be it further

RESOLVED, That these resolutions be spread on the records of the Boston City Hospital and that a copy be sent to the family of Doctor Greenwood and a copy to the *New England Journal of Medicine* for publication therein.

CARMEL R. ALOEN, M.D., *Secretary*
Senior Staff, Boston City Hospital

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

HEMORRHAGE (*Concluded*)

Eight deaths from hemorrhage were associated with separated placenta.

The first case was that of a patient who had had four living children and when a little over eight months along in her fifth pregnancy had a blood pressure of 160 systolic, 100 diastolic, with the appearance of external bleeding. A diagnosis of separated placenta was made, and the patient was treated conservatively by transfusion and an abdominal binder. Forceps effected the delivery of a macerated fetus, the uterus was packed and a transfusion was given; but the patient died of hemorrhage fifty-five minutes later. This was a toxic separation of the placenta associated with intra-partum and post-partum hemorrhage. It is barely possible that hysterectomy, which should have been considered, might have prevented this catastrophe.

The second patient entered the hospital in severe shock due to premature separation of the placenta when approximately thirty-eight weeks pregnant, and died undelivered. She was treated conservatively by vaginal packing and the application of a Spanish windlass. Autopsy revealed premature separation of a normally implanted placenta. This case emphasizes the seriousness of separated placenta; there was no toxemia associated with this fatality, and the patient was given ideal treatment, in spite of which death occurred.

The third patient, with toxemia in her second pregnancy, had a spontaneous separation of a normally situated placenta at the beginning of her thirty-seventh week. Labor started spontaneously, and delivery was accomplished by low forceps. This was followed by excessive bleeding from the

uterus; glucose, plasma and 500 cc. of blood were given, but her blood pressure never returned to normal. This patient was given adequate treatment but died from shock and hemorrhage incident to separation of the placenta.

The fourth case was that of a primipara who began to bleed two weeks before term. A separated placenta was diagnosed, and the membranes were ruptured; but because the bleeding continued and the patient's condition became grave, an emergency cesarean section was performed. A stillborn infant was delivered, but the patient died three hours postoperatively. It is quite likely that this case should have been handled more conservatively from the start. If the vagina had been packed, a Spanish windlass applied and a transfusion given, the result might have been altered.

The fifth patient was a multipara at term in whom bleeding began when she was in labor; a separated placenta was diagnosed. The cervix was said to have been thick, and it was decided to perform a cesarean section. Transfusion was not given, and the patient died shortly after the operation. There seems to be no reason why, in this particular case, conservatism would not have been the better treatment.

The sixth case was that of a primipara who entered the hospital in shock three weeks before term. Her condition improved with treatment, and it was decided to do a cesarean section for separation of the placenta. A living baby was delivered, but the patient died three hours after the operation, autopsy revealing acute dilatation of the heart, probably brought on by the hemorrhage from the separated placenta. There is nothing in the handling of this case that can be criticized: when the patient is not in labor and a living child can be obtained, cesarean section is still considered an intelligent procedure.

The seventh patient had a cesarean section performed at term for complete separation of the placenta. The uterus failed to contract after the operation, and the patient expired from post-partum hemorrhage two hours later. Again, one wonders why hysterectomy was not considered.

The history of the eighth case is not adequate. Separation of the placenta apparently occurred in a toxemic patient who presumably died shortly after a normal delivery.

In 5 cases, death was due to hemorrhage associated with placenta previa.

The first case was that of a patient who was admitted to the hospital with serious hemorrhage at eight months. A complete placenta previa was diagnosed and six transfusions were given, but the patient died a few hours after delivery. This death was probably due primarily to hemorrhage with

superimposed shock. There is little to criticize in the treatment of this case.

The second patient was a multipara with six living children, who began to stain when somewhat over eight months pregnant. She was kept in the hospital for three weeks, when a hemorrhage occurred, the cause of which was diagnosed as placenta previa. Although the patient was not in labor, cesarean section was done; a severe hemorrhage resulted, and she died on the operating table. No transfusion was given.

The third case was that of a multipara who began to bleed at the beginning of the last month of pregnancy. A diagnosis of placenta previa was made by x-ray, and a classical cesarean section was performed; the uterus failed to contract post-operatively, and death occurred five hours after delivery, in spite of transfusions. This patient was hospitalized for fifty days, and it is tragic that such careful prenatal care could not have averted this fatality. The question arises whether hysterectomy in the presence of continued bleeding might not have prevented death if the patient could have stood the operation.

The fourth patient entered the hospital at term, having had three separate attacks of vaginal bleeding before entry. She was not in labor, the fetal heart was audible, and the hemoglobin was 48 per cent. A diagnosis of placenta previa was made, and a cesarean section was performed; but death occurred one hour after delivery from profuse post-partum hemorrhage. It is suggested by the investigator that hysterectomy should have been considered.

The fifth patient, who had had no prenatal care, entered the hospital because of bleeding, the cause of which was diagnosed as complete placenta previa. A cesarean section was performed, and because the bleeding continued after the operation, the abdomen was reopened and the uterus removed. Death, however, occurred twenty minutes following the second operation.

The first of the 2 cases associated with placenta accreta was that of a patient at term on whom a cesarean section was done because of bleeding, a macerated fetus being delivered. Placenta previa was diagnosed at operation, after the placenta was found to occupy the entire lower segment of the uterus. It is probable that the placenta was an accreta since it could not be removed. Supracervical hysterectomy was done, but in spite of this the patient's condition became alarming because of the hemorrhage. Death occurred in spite of transfusion of blood and plasma a few hours after delivery.

The second case was that of a primipara who entered the hospital in labor, having had no prenatal care, and was delivered normally of a still-

born infant. She did not begin to bleed until after delivery of the placenta, which was not intact; the hemorrhage was profuse. The uterus was packed, but death occurred three hours after delivery. Autopsy revealed placenta accreta with uterine apoplexy. This patient was not transfused, nor was the accreta diagnosed until autopsy. Transfusion and intelligent diagnosis of the condition made by uterine examination might have permitted a hysterectomy and subsequent recovery.

Of the 31 patients who died because of hemorrhage, autopsies were performed in only 5.

This review of the cases with hemorrhage as a cause of maternal death reveals the interesting fact that placenta previa is a relatively uncommon cause, and separation of the placenta much commoner. Twenty-five years ago practically all cases of ante-partum bleeding were diagnosed as placenta previa; the existence of a separated placenta was seldom recognized. That two placenta accretas should be diagnosed as the cause of death in 1941 shows a greater appreciation of modern obstetric pathology.

There are few cases in this group in which operative interference or bungling obstetrics was the direct cause of the fatality. This is indeed gratifying. It is, however, unfortunate that many of these patients did not have the benefit of blood transfusion or at least the injection of plasma. The possibility of hysterectomy in certain of these cases needs to be emphasized because repeated transfusions and hysterectomy undoubtedly would have saved the lives of some of these patients.

DEATH

ELLSWORTH — SAMUEL W. ELLSWORTH, M.D., of Quincy, died November 27. He was in his seventy-third year.

He received his degree from Harvard Medical School in 1896 and had served on the staffs of the Quincy City Hospital, the Boston City Hospital and the Massachusetts Memorial Hospitals before specializing in x-ray work.

He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a brother and two sisters survive him.

WAR ACTIVITIES

CIVILIAN DEFENSE

PRACTICE SESSIONS FOR HOSPITALS

The following letter was recently forwarded to all deputy regional hospital heads of the Massachusetts Committee on Public Safety, copies being sent to all regional medical heads and all regional directors:

* * *

It has come to my attention on my trips around the State that the inclusion of hospitals in practice sessions of the mobile medical posts has been rather sadly neglected. To go on the assumption that "it cannot happen here" is simply closing one's eyes to something that one does not

want to see. It CAN happen here and we must be ready for it. Therefore, I urge you very strongly to see to it that you make the hospitals in your region acquainted with the fact that they are to participate in some of the practice sessions of the mobile medical units.

I assume of course that all the hospitals in your region that are to be used for emergency hospitals have already been organized for emergency service. This means that the organization of staffs and personnel has been completed, that the blackout system is completed and that plans have been made with the chief medical officers for the equal distribution of casualties so as not to overcrowd any one hospital.

I know it is difficult to hold these sessions and to mobilize the emergency hospital setup, nevertheless, it must be done to find out how the setup functions in each hospital and only in this way can confusion be avoided when the actual emergency arises. I have seen so much confusion in hospitals during a practice session that, if it were to take place during an actual emergency, it would be at the cost of lives. *This must be avoided.* The inconvenience of practice sessions now will be well worth the effort to achieve the smoother functioning when the time comes.

Will you please see to it that the hospitals in your region and the chief medical officers are so notified. I should also like to have from you at your early convenience a report concerning the progress in this matter.

A WILLIAM REGGIO, Surgeon (R) USPHS
Director, Medical Division
Massachusetts Committee on Public Safety

18 Tremont Street
Boston

INSTRUCTION IN THE DIAGNOSIS AND TREATMENT OF GAS CASUALTIES

Additional changes in the schedule for the six hour course covering the diagnosis and treatment of gas casualties are as follows:

Beverly	January 13
Fall River (not New Bedford)	December 28

MISCELLANY

NOTE

At the fourteenth annual meeting of the New England Obstetrical and Gynecological Society, the following of ficers were elected: Dr Frank A. Pemberton, president, Dr Roy J. Heffernan, vice president, Dr Arthur F. G. Edgelow, secretary, Dr Frederick L. Good, treasurer, Dr Frederick J. Lynch, recorder, Dr Charles J. Kichham, chairman of Executive Committee, Dr John Fallon, chairman of Board of Governors, and Drs Bertram H. Buxton, Frederick L. Good, Adam P. Leighton, H. H. Rosenfield, Louis E. Phaneuf, Charles E. Mongan, John G. Walsh, Joseph W. O'Connor, Alonzo K. Paine, Foster S. Kellogg and Arthur Herug, members of Executive Committee.

CORRESPONDENCE

DEPRIVATION OF LICENSE

To the Editor: This is to inform you that at a meeting of the Board of Registration in Medicine, held on Novem-

ber 20, 1942, the Board voted to revoke the license of Dr William P. Grovestein, of Scituate, Massachusetts, to practice medicine in this commonwealth because of gross misconduct in the practice of his profession, as shown by his conviction in court.

H. QUINBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

REPORT OF MEETING

NEW ENGLAND PATHOLOGICAL SOCIETY

The annual meeting of the New England Pathological Society was held at the Rhode Island Hospital on May 23, 1947. Dr B. Earle Clarke presided.

The first paper, Typhoid Fever, was presented by Drs Goodman, Zouraboff and Fagan, and Miss Annette Rivard. In July, 1938, an outbreak of typhoid fever occurred among a group of 335 disturbed female mental patients, all but one of whom had previously received antityphoid inoculations. The outbreak lasted seven months. In this period twenty (6 per cent) of the exposed patients became ill. Two died, and 10 of the convalescent patients became carriers. In addition, 9 asymptomatic carriers were finally isolated. Of the total of 19 carriers, 10 became chronic whereas 9 were temporary.

From a clinicopathological analysis of data accumulated over a period of almost four years, Dr Goodman concluded that antityphoid immunization does not afford complete protection to all exposed patients, but protects the majority and ameliorates the symptoms in many of the infected group (it has one undesirable feature—namely, that previously immunized individuals may become asymptomatic carriers, difficult to detect because of the absence of clinical evidence of infection), that multiple immunizations seem to increase the patient's sensitivity to the typhoid organism, rather than to augment his resistance to the infection and that a maximum agglutinin response within eight days (average three days) in previously immunized patients is usually associated with a mild clinical course (a maximum agglutinin response after eight days is associated with a prolonged or stormy illness, and this observation may prove to be an aid in prognosis in immunized patients).

Regarding carriers, he said that the terms chronic carrier and temporary carrier should be redefined and suggested that all arbitrary time limits between the two carrier states be abolished on the grounds that they are dangerously misleading and have no physiologic basis in fact. All patients whose gall bladders harbor the *Bacterium typhosum* are regarded as chronic carriers. They are not apt to be intermittent excretors and do not become negative spontaneously. Temporary carriers become negative spontaneously, but may excrete the bacilli for more than a year, with prolonged intervening phases of negativity.

Pre-existing or coexisting cholecystitis and cholelithiasis predispose to the development of the chronic typhoid carrier state. This explains the high incidence of chronic carriers in female patients over the age of forty years, and the tendency of the temporary carrier state to predominate among younger women. It also accounts for the discrepancy between their results and the reports of similar studies in mixed or male communities.

Dr Goodman said that cholecystectomy combined with appendectomy is the only procedure that can be used

tainly suggestive of an exogenous rather than an autogenous source for many of the [staphylococcal] infections."

It has been my clinical experience that infection of the wounds in compound fractures of the skull is minimal during the first forty-eight hours after

the proper therapy of compound fractures of the long bones. The bacteriologic investigation noted above and a host of similar studies not included here answer this objection. Moreover, such work as that by Barnes⁸ and Trueta⁹ on wound infections emphasizes the relative unimportance of

TABLE 1. *Classification of Cases of Compound Fracture of the Skull.*

TYPE OF FRACTURE	ALL CASES			CASES WITHOUT OPERATION			CASES WITH OPERATION					CASES WITH OPERATION CORRECTED FOR TECHNICAL ERRORS				
	NO. OF CASES	NO. OF DEATHS	DEATH RATE %	NO. OF CASES	NO. OF DEATHS	DEATH RATE %	NO. OF CASES	NO. OF DEATHS	DEATH RATE %	SEPSIS No.	SEPSIS %	NO. OF CASES	NO. OF DEATHS	DEATH RATE %	SEPSIS No.	SEPSIS %
Simple compound	153	40 (23*)	26	41	28 (23*)	67	112	12	11	31	28	91	4	4	6	7
Compound, involving the paranasal sinuses and without rhinorrhea	29	11 (0)	38	2	0 (0)	0	27	11	28	6	27	21	6	28	2	10
Compound, involving the paranasal sinuses and with rhinorrhea	12	2 (0)	17	3	1 (0)	33	9	1	11	0	0	9	1	11	1	11
Bullet wound	16	7 (6)	44	9	6 (6)	67	7	1	14	1	14	6	1	17	1	17
Perforating wound	6	0 (0)	0	2	0 (0)	0	4	0	0	1	25	3	0	0	0	0
Avulsion of scalp, with multiple trephinations	2	0 (0)	0	2	0 (0)	0	0	0	0	0	0	0	0	0	0	0
Totals	218	60 (29)	28	59	35 (29)	59	159	25	16	39	25	130	12	9	10	8

*The figures in parentheses indicate the patients dying within twenty-four hours

the injury. I^{5, 6} have therefore repeatedly advocated postponement, for any necessary period up to forty-eight hours, of such major operative procedures as débridement. The postponement should last until after the patient is well out of surgical shock and until he is in an institution where personnel and equipment, including means for multiple blood transfusions, are available. I have always insisted, however, that as a corollary to this the first dressing must be one that only requires an absolute minimal handling of the wound and the débridement, when carried out, must be 100 per cent complete; one must actually excise all contaminated tissue without at the same time either spreading the contamination farther or causing tissue necrosis. Under such conditions, I⁷ have found that it has been possible, provided that those patients whose death, disability or difficulty with wound healing was directly traceable to technical errors arising out of failure to meet these requirements were eliminated, to treat 218 cases of compound fracture of the skull of all kinds with a corrected operative mortality of 9 per cent and a rate of postoperative sepsis of 8 per cent (Table 1). This series includes bullet and perforating wounds, fractures into the various air sinuses, cerebrospinal-fluid rhinorrhea, multiple injuries, associated meningeal hemorrhages and all degrees of brain injury.

Such a concept of bacterial contamination and treatment has been disputed on two main grounds. The first is that the method was not in accord with what was and is often still considered to be

bacterial contamination and the relative value of immobilization of the wound during the first forty-eight hours, whether débrided or not, as a means of preventing this contamination from developing into an infection.

The other criticism has arisen from the fact that no actual study of the bacteriologic contents of the wounds of compound fractures of the skull has been reported and that my theory as applied to this particular problem, although possibly true, had no bacteriologic facts to support it. I believe that the data presented herewith will answer this criticism, particularly since they conform with sufficient accuracy to the more extensive data concerning compound fractures of the long bones, as noted above.

Seventy patients with various types of compound fractures of the skull have had swabs taken from all depths of their wounds as well as from their noses, throats and ears and from two subcortical abscesses. The swabs were then plated for bacteriologic study. In addition, specimens of cerebrospinal fluid and blood were cultured and examined bacteriologically. The patients were divided as follows. In 10, the fracture was compounded not only through the skull but also into one of the paranasal air sinuses—usually the frontal; 6 of these patients died, and all were operated on and drained. In 7 with cerebrospinal rhinorrhea, 2 died. All but one were operated on; 3 cases were drained, and 3 were not, the fistula being closed by way of a transfrontal-flap craniotomy in the latter. Of 7 patients with

bullet wounds, 2 died; 2 were not operated on, 2 others were drained, and 3 were not drained, because the wounds healed by first intention. The bullet was removed in all but the patients who were not operated on, one of whom died of circulatory failure before his general condition war-

brain and 44 from the wound in general, making 112 in all. Because of variables in time and other factors, only cultures that were made from the wounds repay study. Fifty six of these were made on 52 patients. Pathogenic bacteria were grown from 38, or 67 per cent, of these cultures

TABLE 2. *Organisms Recovered from Wounds of Compound Skull Fractures*

ORGANISM	SIMPLE COMPOUND FRACTURES			COMPOUND FRACTURES INVOLVING PARANASAL SINUSES WITHOUT RHINORRHEA			COMPOUND FRACTURES INVOLVING PARANASAL SINUSES WITH RHINORRHEA			BULLET WOUNDS			PERFORATING WOUNDS			ALL FRACTURES		
	RECOV- ERED CASES	FA- ILED CASES	TO- TAL CASES	RECOV- ERED CASES	FA- ILED CASES	TO- TAL CASES	RECOV- ERED CASES	FA- ILED CASES	TO- TAL CASES	RECOV- ERED CASES	FA- ILED CASES	TO- TAL CASES	RECOV- ERED CASES	FA- ILED CASES	TO- TAL CASES	RECOV- ERED CASES	FA- ILED CASES	TO- TAL CASES
<i>Str. haemolyticus</i>	1	2	3	0	0	0	0	0	0	0	0	0	0	0	0	1	2	3
<i>Str. haemolyticus</i> and <i>Staph. aureus</i>	2	1	3	0	1	1	1	0	1	0	0	0	0	0	0	3	2	5
<i>Staph. aureus</i>	21	0	21	0	1	1	2	0	2	2	2	4	1	0	1	26	3	29
<i>Staph. albus</i>	7	0	7	0	0	0	0	0	0	0	0	0	0	0	0	7	0	7
<i>Meningococcus</i>	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1
No growth	9	0	9	1	0	1	1	0	1	0	0	0	0	0	0	11	0	11
Total	40	3	43	1	3	4	4	0	4	2	2	4	1	0	1	48	8	56

ranted operation. The other is alive and well a year after his injury, although the bullet remains lodged in the base of his skull between the jugular bulb and the internal carotid artery. The arteriovenous fistula caused by its presence there has been closed by a ligation of the common carotid artery in the neck. Two patients with perforating wounds were operated on and survived, neither wound being drained. One of these patients had a previously unrecognized olfactory-groove meningioma at the time of his injury. This was removed after a subcortical abscess, which developed as the result of the improper treatment of the stab wound, had been healed up. Finally, there were 44 uncomplicated compound fractures. Four patients died, all following operation. Three others were not operated on. Eight patients, including 3 who died, had sepsis following operation. In 5 of these 8, including 2 of the deaths, the death and postoperative sepsis were directly traceable to improper therapy: 2 patients were operated on after the forty-eight-hour limit had passed, 2 had inadequate débridement, and in 1, tissue necrosis developed because of stitches that were too tight.

The cultures were grouped as follows: 1 from the ear, 4 each from the nose and throat, 2 from subcutaneous abscesses, 11 from the blood, 38 from the cerebrospinal fluid, 4 from the exposed calvarium, 4 from the dura, 4 from the wounds in the

All the bacteriologic work in this series was done under the direction of Dr. Robert N. Nye, assistant pathologist, and Miss Marion E. Lamb, bacteriologist, of the Mallory Institute of Pathology, Boston City Hospital. In accordance with the custom of the Bacteriology Laboratory, streptococci were reported only when they were of the pathogenic type. *Staph. aureus*, when reported, was also considered pathogenic, but *Staph. albus* even though reported, was considered nonpathogenic, as were *Aerobacter aerogenes*, diphtheroids, and "spreaders." Pneumococci and meningococci were both reported and considered to be pathogenic, of course. *Escherichia coli* was reported once. At autopsy, it was found that the patient had died of *Esch. coli* meningitis. No attempt was made to culture any anaerobes. Aerobic cultures (blood broth and blood-agar plates) were incubated seventy-two hours, and if no bacteria had grown by the end of that time, a report of "no growth" was made. It is not suggested, and I do not believe, that the wounds whose cultures showed "no growth" were sterile. I believe there can be no doubt that all the wounds contained bacteria. However, the contamination was so slight in many that the swab did not come in contact with any of the contaminants.

Of the 38 cultures of pathogenic bacteria, 29 (76 per cent) showed *Staph. aureus* only, 3 (8 per cent) *Str. haemolyticus* only, and 5 (13 per cent)

a mixture of both (Table 2). Meningococci were grown from only 1 culture. If these figures are broken down still further, particularly in relation to the time elapsing between the infliction and swabbing of the wound, certain other significant data are apparent. Thirty-one wounds were swabbed within twenty-four hours or less of the receipt of injury. Of this group, 17 (55 per cent) showed pathogenic bacteria. No pure cultures of hemolytic streptococci were grown, and only 2 of mixed hemolytic streptococci and *Staph. aureus*. The remaining 15 all showed pure *Staph. aureus*. Forty-four wounds were forty-eight hours old or less when cultured. Twenty-six (66 per cent) grew pathogenic bacteria. Of these, 1 (4 per cent) grew *Str. haemolyticus*, and 4 (15 per cent) a mixture of this organism and *Staph. aureus*. The remaining 21 showed pure *Staph. aureus*. Twelve wounds were cultured when they were over forty-eight hours old. Eleven, or 91 per cent, contained culturable pathogenic bacteria. Thus, the percentage of compound fractures of the skull that contained cultural pathogenic bacteria within the wounds rose from 55 in the first twenty-four hours through 66 in the first forty-eight hours to 91 after forty-eight hours had elapsed between the receipt of the wound and its swabbing for culture. The conclusion seems inescapable from these figures that the rate of contamination of such wounds is essentially stationary for forty-eight hours after their infliction, but that thereafter it rises rapidly to the neighborhood of 100 per cent.

There were 7 patients from whose wounds hemolytic streptococci were cultured eight times. Three of the cultures were pure, and the rest were mixed with *Staph. aureus* alone twice and with both that and *Staph. albus* three times. Three wounds were cultured at operation, and only 2 of these within twenty-four hours of the infliction of the wound. One of the latter patients had a very extensive compound fracture of the frontal bone, with practically complete destruction of the posterior wall of one frontal sinus and a wide-open communication between the nose and the meningeal spaces. The other had a simple compound fracture. The wound had been treated only by covering with a sterile gauze pad. This is the sole case in which the streptococcus might have been introduced at the time the wound was made. The patient was struck about the head and face by an assailant who used an iron bar. The skull was fractured in the right parietal and left temporal regions. Another culture, made from this wound fourteen days postoperatively, was also positive for hemolytic streptococci. This patient survived. In the third patient and the 4 succeeding ones, all the wounds were cultured forty-eight or more hours after infliction. The third patient was an-

other whose fracture was compounded not only externally but also into a frontal sinus. He was not brought to the hospital until twenty-four hours after he had been injured. The wound was cultured forty-eight and débrided fifty-five hours after infliction. Meningitis was already present when the débridement was performed. This patient died. The other cultures were made two, two, ten and twelve days after infliction, or one, one, nine and eight days after operation. In view of the time that elapsed between the injury and the postoperative culture, there was ample opportunity for implantation of streptococci into these last five wounds after their infliction and before they had been cultured or débrided. Of these 5 patients, 4 died, 2, partly at least, because débridement was postponed for fifty-five hours in one case and was not done at all in the other, with the result that meningitis supervened in the first and a cortical abscess in the second. Death in the other 2 cases was from meningitis, despite the fact that all technical requirements had been met. The fifth patient survived in spite of a complicating meningitis. The technic used was satisfactory. No throat or nose cultures were made from any of these 7 patients.

In 1 patient, meningococci were cultured from the wound seven days after its infliction and one day after operation. The fracture in this case was compounded through the frontal bone and also into one frontal sinus. At operation, six days after the injury, the wound was irrigated. The patient died of meningitis and a frontal-lobe abscess. The meningococcus certainly originated in the nose and was spread by the irrigation.

Pneumococci were cultured from 3 patients. All had fractures compounded into the nose, 1 by way of one frontal sinus and the other 2 by way of the cribriform plate, both the latter being accompanied by cerebrospinal rhinorrhea. The first patient was not operated on, and the pneumococcus was cultured from the cerebrospinal fluid ten days after the injury and in the presence of a meningitis. The second case was similar in that no operation was performed, but the bacterium was cultured from the cerebrospinal fluid four days after the injury. A positive blood culture was obtained in this case at the same time. Sulfapyridine had been given by mouth from the start. Both these patients died. In the third patient, the cerebrospinal-fluid fistula was closed within twenty-four hours of the injury by way of a transfrontal bone-flap operation. Just previous to this, a culture of the nose had proved positive for pneumococci. The wound healed by first intention, and the patient recovered. None of the sulfonamide group of drugs were used in this case.

There were 3 deaths among the patients from whose wounds *Staph. aureus* was grown. All were directly traceable to errors in technic. In 1 case, meningitis followed forcible removal of a Mosher cone-shaped copper-wire drain about three weeks after operation for a compound fracture of the frontal bone that involved one frontal sinus; another patient died of *Esch. coli* meningitis following a débridement that was not done for sixty hours after the accident; this patient was given sulfapyridine by mouth. In the third patient, who had a bullet wound, the débridement had to be postponed for forty-eight hours because of the patient's general condition. Sulfapyridine was given by mouth and sulfanilamide put in the wound from the first, and the wound was closed at operation. The patient died from meningitis. Three other patients recovered but had sepsis in their operative wounds. In 2 cases, no cause for the sepsis could be found in the technic, but in the third,—a perforating wound, in which débridement was not done,—a cortical abscess followed.

There were 20 wounds in which the cultures were reported as showing either no growth or *Staph. albus*. Three of these patients died—all in the "no growth" group. Two wounds were compound fractures of the frontal bone, with extension into one frontal sinus. One patient, who was not operated on, died of pneumococcal meningitis, and the other died four days after operation of a meningitis whose cause was not identified. The third patient, with a bullet wound, died of circulatory failure before he could be operated on. Four other patients, who recovered, had sepsis or wounds that failed to heal by first intention. The sepsis was traceable to technical errors in every case. One, with a compound fracture of the frontal bone and involvement of the frontal sinuses, who was not operated on until six days after injury, developed a secondary frontal subcortical abscess, which later had to be drained. Another, with an uncomplicated compound fracture, was not brought to the hospital until sixty hours after injury, and although the wound was partially débrided two hours later, it was considered better judgment to pack the wound and allow it to heal by second intention rather than to close it at once. The third patient—a similar case to the last—was not brought to the hospital for five days. No operation was performed, the wound being merely packed wide open. The last case was also an uncomplicated compound fracture in which it was decided to substitute chemotherapy for surgery—sulfapyridine was administered by mouth and sulfanilamide put in the wound. The wound granulated but refused to heal completely until, at the end of two weeks, exploration disclosed a "rock" of sul-

fanilamide. This was removed, after which the wound healed promptly. There were no deaths or sepsis among the 9 patients from whose wounds cultures yielded *Staph. albus* only.

DISCUSSION

It appears from this material that the degree of culturable contamination of the wounds of compound fractures of the skull varies from 55 to 66 per cent during the first forty-eight hours after infliction, provided the wound is not "massaged" during that period. The rise during the second twenty-four-hour period is statistically minimal, and it probably makes little difference at what time during this forty-eight-hour period the débridement is done, provided it is 100 per cent complete. If these requirements are fulfilled, and particularly if inhibition of further growth of bacteria is aided by proper chemotherapy, postoperative infection of such wounds should be reduced to something closely approximating that seen after uncontaminated surgical wounds anywhere in the body. The contention that pathogenic hemolytic streptococci are not deposited in the wound at the time of its infliction, as advanced by Hare and Willits² and others in compound fractures of the long bones, must be considered to hold true also in compound fractures of the skull with one exception. This refers to fractures that involve the paranasal sinuses and applies not only to hemolytic streptococci but also to meningococci and pneumococci. Except for multiple small perforating wounds, with many fragments of foreign bodies scattered throughout the substance of the brain, I see no reason so far as this experience goes, to differentiate either bacteriologically or therapeutically bullet wounds from other types of compound fractures of the skull. This is in general accord with recent experience with compound fractures of the long bones as cited by Trueta⁹ and others. Moreover, this evidence supports the contention of Trueta and of Barnes⁸ that immobilization of the wound is the critical factor if, for immobilization, one means a "minimum of handling at the first dressing of the wound" and until the débridement is done. It must be evident that this dictum is much more important and more in accord with the established facts than any shibboleth that is based on tradition. There is no "golden six-hour interval" in which surgery of compound fractures of any bone whether long or flat must be practiced. If the bacteria contaminating a wound are "stirred with a spoon" or the tissues contaminated by these bacteria are "massaged," a thirty-minute interval between infliction and débridement is too long to wait before one deals with the infection that has been conjured up

out of what was only a contamination. If the contamination is recognized for what it actually is and treated with the respect it merits, infection can be prevented from developing by a proper débridement carried out at any time within the first forty-eight hours after infliction of the wound, provided the patient is safely out of surgical shock and in a properly equipped and staffed hospital.

SUMMARY

A report of 112 cultures made from 70 patients with varying types of compound fractures of the skull is presented.

Fifty-six wound cultures were taken in 52 cases. The incidence of infection in the wounds of these compound fractures of the skull was 55 per cent during the first twenty-four hours, 66 per cent during the first forty-eight hours, and 91 per cent after forty-eight hours had elapsed between infliction and swabbing of the wound.

Pathogenic hemolytic streptococci were grown from the wounds of only 7 patients, in only 1 of whom there was evidence that the contamination could reasonably have taken place at the time of infliction of the wound.

These results conform in general to those obtained from the study of certain series of wounds in other parts of the body received in military action, in the course of air-raids and in civil life.

They emphasize the value of immobility of the wound or its equivalent in all compound fractures as a means of preventing contamination from becoming infection, and the lack of significance of the local growth of bacteria as the cause of this change.

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PLASMA PROTHROMBIN AND LIVER FUNCTION DURING SULFONAMIDE THERAPY*

ISRAEL KAPNICK, M.D.,† JOHN D. STEWART, M.D.,‡ AND CHAMP LYONS, M.D.§

BOSTON

THERE have been described two types of injury to the liver resulting from therapy with the sulfonamides. Jaundice and signs of diminished hepatic function may accompany the acute hemolytic crises that occasionally occur following the administration of these drugs. Secondly, a primary hepatitis may result as a direct toxic effect of the chosen drug on the liver cells.

The acute hemolytic crisis with a rapidly progressive anemia may come on at any time following the onset of drug administration, and usually occurs within three to five days. Wood¹ found the anemia to occur only in febrile patients. The hemoglobin may fall rapidly to 20 to 30 per cent of normal, and this is accompanied by a rise in temperature, polymorphonuclear leukocytosis, reticulocytosis and an increase in immature cells, with evidence of hyperactivity of the hematopoietic system. Hemoglobinuria may occur.² In some

cases this is accompanied by jaundice, with evidence of hepatitis and diminished hepatic function. The hepatitis may be mild and clear up rapidly after the drug is stopped. The severe cases may go on to acute yellow atrophy and death. The presence of jaundice in hemolytic anemia has been ascribed mainly to the hemolytic process, but direct liver damage may coexist with it.³

There have been a number of reports indicating an apparent primary acute toxic hepatitis with jaundice and decreased liver function during or subsequent to sulfonamide therapy, with several deaths. The importance and the serious nature of this complication are indicated by the fact that nearly all the fatalities resulting from the sulfonamide drugs have been due to agranulocytosis, toxic hepatitis or hemolytic anemia. Hageman and Blake⁴ noted 1 case of toxic hepatitis with recovery in a group of 114 patients receiving sulfanilamide, and Bannick, Brown and Foster⁵ reported 2 deaths. Cline⁶ reported autopsy findings of acute yellow atrophy following the administration of 45 gm. of sulfanilamide. Saphirstein⁷ had a severe but nonfatal case of toxic hepatitis following the use of this drug, with an associated der-

*From the Surgical Research Laboratories of the Harvard Medical School at the Massachusetts General Hospital, Boston.

†Formerly, research fellow in surgery, Harvard Medical School, and graduate assistant in surgery, Massachusetts General Hospital.

‡Formerly, assistant in surgery, Harvard Medical School, and assistant surgeon, Massachusetts General Hospital.

§Assistant surgeon, Massachusetts General Hospital; associate in surgery and instructor in bacteriology, Harvard Medical School.

matitis which was exfoliative in character. This has been seen to accompany the hepatitis in several other cases reported in the literature. Garvin⁸ reported 5 cases with 1 death, and Berger and Applebaum⁹ reported autopsy findings of subacute liver atrophy following sulfanilamide. Other cases of toxic hepatitis have been reported by Ottenberg,¹⁰ Fitzgibbon and Silver,¹¹ Gertler¹² and Russell.¹³ A fatal case reported by Tragerman and Goto¹⁴ showed degeneration of the liver cells. Greene and Hotz¹⁵ mention 4 cases of hepatitis with 2 deaths, and found an increase in the sulfanilamide level in the liver in a patient with hepatitis. Spring and Bernstein¹⁶ reported 2 cases in which there was a coexistence of toxic hepatitis with acute hemolytic anemia and renal damage following sulfanilamide.

Long, Haviland, Edwards and Bliss¹⁷ found that the incidence of toxic hepatitis, as indicated by jaundice without anemia and a definite impairment of liver function, occurred in 0.6 per cent of 1000 hospitalized adults receiving sulfanilamide therapy. Many other authors have noted mild attacks of jaundice without anemia, which usually subsided rapidly on discontinuation of the drug. The incidence of these occasional complications is not inappreciable. Jaundice appears to be commoner after sulfanilamide than after other drugs of the sulfonamide series.

Hepatitis may occur early or late in the course of therapy, and may even first be observed up to six days after the drug has been discontinued. In most of the cases reported the dosage has not been particularly large, and in almost all cases was below 50 gm. The hepatitis may take the form of toxic necrosis or of acute yellow atrophy. Jaundice, hepatomegaly, splenomegaly and ascites may occur. There is usually an immediate direct van den Bergh reaction, increased urobilinogen in the urine and decreased hepatic function. Often a high temperature and leukocytosis occur with the hepatitis, and the patient is acutely ill. In mild cases the prognosis is usually good if the drug is immediately stopped, fluids forced and supportive treatment instituted. However, the hepatitis may progress in spite of the discontinuance of the drug, as illustrated by 2 of the cases presented by Garvin.⁸

MATERIALS AND METHODS

All patients studied in the present series were on the surgical wards of the Massachusetts General Hospital in the spring and summer of 1941, and had infections of the average type found on a general surgical service. These included cellulitis, abscess, carbuncle, thrombophlebitis, bacteremia, urinary infection, osteomyelitis, acute pulmonary and pelvic infections, and ulcer. About half the patients were acutely ill with marked febrile reac-

tions; the remainder had more chronic, less virulent infections. The drugs used were sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine. The dosages varied from as little as 3 to 8 or 9 gm. per day.

The liver-function tests selected for study were the bromsulfalein excretion, the van den Bergh reaction and the prothrombin time. The Quick¹⁸ technic was used for this latter test.

It has been pointed out that reduction in the plasma-prothrombin level may be an early and very sensitive indication of decline in hepatic reserve.¹⁹ Wilson²⁰ found a close correlation between the level of plasma prothrombin and the hippuric acid liver-function test. In patients with liver damage these two were more sensitive measures of hepatic damage than any other liver-function test. However, in any toxic reaction to the liver it is possible that the different functions of this organ may be affected to a varying extent. One function may show severe incompetence, while another is completely unaffected.

The tests in our series were carried out before the drug was begun, and at intervals until several days after the drug was discontinued.

DATA

Sixty-eight patients in all were studied, and of these 14, or 21 per cent, showed an appreciable increase in prothrombin time during the course of chemotherapy. Only a few of the latter showed changes in bromsulfalein excretion or in the van den Bergh reaction. No patient showed changes in these latter two without, in addition, showing a fall in the level of plasma prothrombin.

The cases with significant increases in prothrombin time are abstracted below.

CASE REPORTS

CASE 1. J. P., a 39-year-old Finnish housewife with known biliary cirrhosis of 2 years' duration, was admitted for study of generalized xanthomatosis of 2 months' duration. She had been under treatment with parenteral and oral vitamin K for 9 months because of a prolonged prothrombin time. A biopsy of one of the xanthomatous nodules was performed, and 6 days later the patient developed a cellulitis and erysipelas, with redness, pain, lymphadenitis, a temperature of 103.4°F. and a white-cell count of 19,100. Cultures of the leg showed a virulent beta hemolytic streptococcus (Group A, Lancefield) and coagulase-positive *Staphylococcus aureus*. In view of the liver damage it was thought that chemotherapy was inadvisable, but the patient developed a chill and extension of the clinical signs of infection. The prothrombin time was 21 seconds (21 seconds*) and the van den Bergh reaction was 5.4 mg. per 100 cc. The patient was given 6 gm. of sulfanilamide initially, then 1 gm. every 4 hours. She was also given 32,000 units of scarlet-fever antitoxin and an immune transfusion because of the absence of opsonic antibodies from the blood. The infection improved rapidly but on the seventh day of chemotherapy

*All figures in parentheses indicate the normal prothrombin time.

the prothrombin time was 85 seconds (23 seconds) and the van den Bergh reaction was 6 mg. per 100 cc. The chemotherapy was stopped and intravenous vitamin K was given. Within 24 hours the prothrombin time was normal.

CASE 2. L. T., a 64-year-old Negress, had a radical mastectomy for adenocarcinoma. Postoperatively she developed a staphylococcal infection of the wound, which was drained. She appeared to be doing well but suddenly developed erysipelas, with a temperature of 105°F. and redness and an erysipeloid reaction about the wound. The prothrombin time and van den Bergh and bromsulfalein tests were all normal. The patient was given 4 gm. of sulfapyridine initially, then 1 gm. every 4 hours. She also received 32,000 units of scarlet-fever antitoxin and an immune transfusion. A blood culture showed two colonies per cubic centimeter of beta hemolytic streptococcus (Group A). The temperature returned to normal in 48 hours. On the 3rd day of chemotherapy the prothrombin time was 29 seconds (23 seconds), the van den Bergh reaction was negative, and the bromsulfalein test showed a 5 per cent retention. On the 7th day of chemotherapy the prothrombin time was 32 seconds (23 seconds), the van den Bergh reaction was negative, and the bromsulfalein test showed a 12 per cent retention. The drug was discontinued, and on the 10th day all the tests were normal.

CASE 3. M. D., a 38-year-old housewife, was admitted for repair of a ureterovaginal fistula. At operation the ureter was implanted into the dome of the bladder and sulfanilamide powder was placed in the wound. On the 3rd postoperative day the patient developed pyelitis. A blood culture taken at this time yielded *Escherichia coli*. The prothrombin, van den Bergh and bromsulfalein determinations were all normal. Sulfapyridine was given in a dosage sufficient to maintain a blood level of between 10 and 12 mg. per 100 cc. On the 4th day of chemotherapy the prothrombin time was 38 seconds (23 seconds), the van den Bergh reaction was negative, and the bromsulfalein retention was 8 per cent. On the 5th day of chemotherapy the prothrombin time was 38 seconds (23 seconds). The chemotherapy was omitted and Hykinnone was given parenterally. Twenty-four hours later the prothrombin time was normal. Four days later the bromsulfalein retention and the van den Bergh reaction were also normal.

CASE 4. J. C., a 43-year-old Negro, entered the hospital with bilateral chronic pulmonary suppuration, apparently not tuberculosis, and a secondary pneumonia. The blood Hinton test was positive, and there was evidence of cardiovascular syphilis with an aneurysm. The control prothrombin time was 25 seconds (22 seconds) and the van den Bergh and bromsulfalein determinations were negative. The patient was started on 4 to 6 gm. of sulfathiazole daily. On the 5th and 9th days of therapy the prothrombin time was 30 seconds (22 seconds). At this time the drug was changed to sulfapyridine, 4 gm. daily. After 5 days the prothrombin time was 30 seconds (23 seconds), the van den Bergh determination showed a trace, and the bromsulfalein retention was 5 per cent. Chemotherapy was discontinued because of no results. Three days later the prothrombin time was 24 seconds (22 seconds).

CASE 5. L. H., a 37-year-old chauffeur, entered with a 5-day history of abdominal pain, anorexia, nausea and vomiting. Examination revealed a mass in the right

lower quadrant of the abdomen, and a diagnosis of a perforated appendix with abscess was made. The appendiceal abscess was drained, and an appendectomy was done. Sulfapyridine was placed in the wound and was given intravenously in a dosage to maintain a blood level between 8 and 9 mg. per 100 cc. The control prothrombin time was 25 seconds (23 seconds), a bromsulfalein test showed 7.5 per cent retention, and the van den Bergh reaction was 2.4 mg. per 100 cc. On the 2nd day of chemotherapy the prothrombin time was 32 seconds (23 seconds); 3.2 mg. of Hykinnone was given. On the 4th day the prothrombin time was 37 seconds (23 seconds), the bromsulfalein retention was 5 per cent, and the van den Bergh reaction was 2.6 mg. per 100 cc. Chemotherapy was discontinued at this time owing to drug fever. The prothrombin time gradually returned to normal, and on the 11th day after the drug was stopped it was 26 seconds (23 seconds) and the van den Bergh determination was 1.7 mg. per 100 cc.

CASE 6. R. H., an 8-year-old Negro, blind since birth, was admitted because of a furuncle of the leg and septicemia. A blood culture yielded a coagulase-positive *Staph. aureus*. The control prothrombin and van den Bergh determinations were normal. The patient was started on sulfathiazole, with a dosage of 6 to 9 gm. daily. He developed a subperiosteal abscess of the tibia, which was drained with ligation of the femoral vein. He then showed evidence of pulmonary miliary tuberculosis. The prothrombin time gradually increased, and on the 15th day of chemotherapy it was 38 seconds (22 seconds) and the van den Bergh reaction was 2.4 mg. per 100 cc. Hykinnone was given at this time, and the prothrombin time returned to normal within 24 hours and remained so until death 4 days later from acute tuberculosis. Shortly before death the van den Bergh was 2.8 mg. per 100 cc. and the bromsulfalein test showed 20 per cent retention.

CASE 7. L. W., a 53-year-old woman, was admitted with a septic prepatellar bursitis, which had developed 2 weeks after a fall. A culture yielded an attenuated microaerophilic beta hemolytic streptococcus (Group A) and a coagulase-positive staphylococcus. The control prothrombin time was 21 seconds (23 seconds), the van den Bergh reaction showed a trace, and the bromsulfalein test was negative. The knee was drained, and the patient was started on sulfanilamide, with a dosage of 4 gm. initially and 6 gm. daily for 8 days, blood levels between 9 and 11 mg. being obtained per 100 cc. On the 6th day of chemotherapy the prothrombin time was 34 seconds (22 seconds), and on the 8th day it was 37 seconds (22 seconds). The van den Bergh and bromsulfalein determinations remained normal throughout. The drug was discontinued because the patient developed a rash, the urine was loaded with sulfanilamide crystals and young red and white cells were present in the blood. Two days later the prothrombin time was 28 seconds (22 seconds); 3 days later it was 24 seconds (22 seconds).

CASE 8. D. W., a 9-year-old girl, was admitted with a diagnosis of osteomyelitis of the knee and staphylococcal bacteremia. She had received chemotherapy prior to admission. The control prothrombin time was 31 seconds (22 seconds), and the van den Bergh reaction was negative. The patient was started on large doses of sulfadiazine, 9 to 11 gm. per day, and the usual supportive treatment. After 5 days the prothrombin time was nor-

ml and showed no further change, in spite of large amounts of sulfadiazine.

CASE 9 W W, a 23 year-old man, was admitted with a diagnosis of acute gonococcal urethritis and a possible arthritis. The control prothrombin time, van den Bergh, and bromsulfalein reactions were all normal. He was started on a dosage of 6 gm of sulfathiazole daily. After 21 days of chemotherapy the prothrombin time was 31 seconds (22 seconds). The drug was omitted, and the prothrombin time returned to normal within 43 hours.

CASE 10 L F, a 46-year-old woman, was admitted with a diagnosis of pelvic inflammatory disease and peritonitis. The control prothrombin, van den Bergh and bromsulfalein tests were all normal. Treatment with sulfapyridine was begun, and later the patient was shifted to sulfathiazole. On the 12th day of chemotherapy the prothrombin time was 31 seconds (22 seconds), on the 14th day it was 34 seconds (22 seconds). The patient became acutely ill, developed thrombophlebitis of the pelvic veins, and was heparinized. Two days after heparin was discontinued, the prothrombin time was 70 seconds (22 seconds) and the van den Bergh reaction was 2.4 mg per 100 cc. Two days later the prothrombin time was 51 seconds (22 seconds), the van den Bergh reaction was 3 mg per 100 cc, and the bromsulfalein test showed 20 per cent retention. The following day the prothrombin time was 32 seconds (22 seconds), the van den Bergh reaction was 2.2 mg per 100 cc, and the bromsulfalein test showed 20 per cent retention. At this time treatment was begun with vitamin K, and 4 days later the prothrombin time was normal, but the bromsulfalein reaction did not return to normal until 1 week later, at which time there was a trace in the van den Bergh reaction.

CASE 11 E L, a 23 year-old man, was admitted for a pneumonectomy for bronchiectasis, at which time sulfanilamide powder was placed in the pleural cavity. The control prothrombin, van den Bergh and bromsulfalein determinations were all normal. The patient was started on 6 gm of sulfapyridine daily. On the 5th day of chemotherapy the prothrombin time was 30 seconds (22 seconds), on the 8th day it was 35 seconds (22 seconds). On the 10th day microscopic hematuria developed and the drug was stopped. Six days later the prothrombin time was 29 seconds (22 seconds). Three days later it returned to normal. The van den Bergh and bromsulfalein determinations remained unchanged throughout.

CASE 12 J C, a 36-year-old man, was admitted for resection of a chondrosarcoma of the sternum, which was complicated postoperatively by pneumonia. The prothrombin time was 25 seconds (22 seconds), and the van den Bergh and bromsulfalein determinations were normal. Sulfapyridine therapy was begun. On the 4th day of chemotherapy the prothrombin time was 33 seconds (22 seconds), the van den Bergh reaction was 1.6 mg per 100 cc, and the bromsulfalein test showed 5 per cent retention. Chemotherapy was stopped at this time. The patient died the following day.

CASE 13 T P, a 39 year-old policeman, entered with a diagnosis of cellulitis of the scalp. The prothrombin time was 24 seconds (22 seconds), the van den Bergh reaction showed a trace and the bromsulfalein retention was normal. Three grams of sulfathiazole was given initially. A culture of the wound yielded an attenuated beta hemolytic streptococcus (Group A) and a coagulase positive staphylococcus. The drug was changed to 8 gm of sul-

fanilamide daily, which maintained a blood level between 9 and 12 mg per 100 cc. On the 2nd day of chemotherapy the prothrombin time was 28 seconds (22 seconds), and on the 5th day it was 30 seconds (22 seconds). At this time the dosage was halved. In 2 days the prothrombin time was 26 seconds (22 seconds), the van den Bergh determination showed a trace, and the bromsulfalein test showed 5 per cent retention. Shortly after this the patient developed bilateral deep phlebitis with a positive Homans's sign, which was partially relieved by a paravertebral novocain block. Chemotherapy was omitted, and 3 days later the temperature went to 104°F and the patient developed an acute hemolytic anemia, with a red-cell-count drop to 1,700,000. The prothrombin time was 32 seconds (22 seconds). Three transfusions were given, and the hemolytic crisis lasted only about 24 hours. The prothrombin time returned to normal in 4 days.

CASE 14 J R, a 28 year-old man, was admitted with a carbuncle of the neck and a *Staph aureus* bacteremia. The temperature was 106°F on admission but the prothrombin time and van den Bergh reaction were normal. The patient was started on sulfadiazine, 9 to 12 gm daily, to maintain a blood level between 15 and 20 mg per 100 cc. The day following admission he developed a thrombophlebitis of the side of the neck and pleuritic chest pain. Accordingly ligation of the external and internal jugular and middle thyroid veins was carried out and the carbuncle was excised. On the 5th day of chemotherapy the prothrombin time was 30 seconds (22 seconds). The patient recovered.

DISCUSSION

Watson and Spink³ did not observe jaundice in any adult receiving less than 3 gm of sulfanilamide per day, and no increase of urinary urobilinogen in these cases. We found no change in prothrombin level in any case receiving 4 gm or less of sulfonamide per day. When daily doses of 4 to 8 gm are given, it is obvious that in a considerable proportion of patients there is a definite decrease in the plasma prothrombin level. Most of these patients were acutely ill and highly toxic, and many had high temperatures. However, fever alone was not accompanied by a decrease in the prothrombin level. Many of our patients were taking little food by mouth and were being sustained with parenteral fluids. Because of the short period of time involved, it is unlikely that inadequate dietary intake was a factor in the decrease of plasma prothrombin. Whether prothrombin deficiency can occur in man solely on the basis of insufficient food intake is still doubtful.¹⁰

The type of infection seemed to make no difference in these cases. It is well known that toxic hepatitis, with jaundice and reduction in plasma prothrombin, may occur in severe infections or in chronic sepsis.^{10, 21} The cause is unknown, although this complication appears to be commoner in cases of peritoneal sepsis. Hence, in these cases both the infection and the chemotherapy exert a hepatotoxic effect. That the infection may play a

considerable accessory role in the depression of liver function is shown by the fact that patients on chemotherapy who had severe infections showed changes in prothrombin levels much more frequently than did those with minor infections.

In the cases reported in the literature only 1 has had serologic evidence of syphilis, and only 1 of ours was similarly affected. Hence this does not appear to be a factor.

In our cases, depression of the plasma-prothrombin level occurred with all four of the drugs used—sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine. We do not have enough cases to warrant any statistical analysis concerning the relative frequency with which this occurs with the different drugs. However, sulfadiazine was used in only 1 of our cases with an increased prothrombin time, and this was quite mild. In another case, there was a depression of prothrombin level with sulfathiazole, which cleared up on discontinuance of the drug and did not recur later on when sulfadiazine was given.

In most cases, depression in prothrombin level did not occur until the drug had been used for four or five days. In 1 case, however, it occurred forty-eight hours after the drug was begun. In most cases the prothrombin levels returned to normal within a few days after the drug was discontinued. In 1 case, however, a week was necessary.

There is probably an increased incidence of hepatitis in patients with previous liver damage or alcoholism. In 1 of our patients, who had a severely damaged liver, there was a sudden and marked fall in prothrombin level when chemotherapy was begun. However, in most cases, chemotherapy can be continued for some time with little or no effect on the liver. A sulfonamide drug has been given to patients with cirrhosis or jaundice without untoward results.²²

None of our patients developed jaundice and clinical evidence of toxic hepatitis. This may have been due to the fact that the drug was discontinued or used with great caution in those patients who showed changes in the plasma-prothrombin level. In all cases this level returned to normal after stopping of the drug, and there was no evidence of any permanent impairment of liver function. In all cases in which parenteral vitamin K was given, the prothrombin time was normal within twenty-four hours, indicating that the liver was able to respond.

Usually the first sign noted clinically that warns the physician of the occurrence of toxic hepatitis is the appearance of jaundice. By this time it may be too late to prevent a fatality or a major illness superimposed on the patient's infection, even if the drug is promptly stopped. Weir²³ has pointed out

that hepatitis, even to the extent of fatal acute yellow atrophy, can occur without jaundice. Slowly progressive changes in the liver may follow a bout of acute hepatitis in spite of apparent complete recovery, and advanced cirrhosis may follow an old acute hepatitis that never produced any clinical symptoms.²⁴ Since changes in the prothrombin level appear to be an early indication of impending liver damage, the test is of great help in avoiding this major complication.

Although the cause of the hepatitis following sulfonamide therapy is unknown, two possibilities have been considered. It may be another example of drug hypersensitivity, which occurs in an occasional patient owing to idiosyncrasy, or these drugs may regularly produce evidence of hepatic dysfunction. In the case cited by Fitzgibbon and Silver¹¹ and in several others in the literature, there was an interval of several weeks between courses of the drug, and this suggests the former explanation. However, since so many cases show some evidence of liver damage, it is clear that these drugs are inherent liver poisons. A severe hepatitis is probably an accentuation of a usual toxic effect rather than a true drug idiosyncrasy. However, both these factors may play a role in certain cases.

Probably all factors that tend to depress liver function will exaggerate the effects of the sulfonamides in reducing liver function. Hence all possible measures to maintain liver reserve should be taken in patients receiving chemotherapy. It has recently been shown that a high-protein (casein) diet protects rats being given large amounts of sulfanilamide daily.²⁵

CONCLUSIONS

Liver function, as measured by prothrombin, van den Bergh and bromsulfalein tests, was measured in 68 patients receiving sulfonamide therapy for acute infections. Fourteen patients, or 21 per cent, showed a significant decrease in the prothrombin level during chemotherapy. The severity of the infection seemed to be more significant as the cause of prothrombin depression than did the type of sulfonamide used. It is recognized that decreased prothrombin time may be the consequence of factors other than impaired liver function. Inasmuch as serious infection and sulfonamides are both prejudicial to the welfare of the liver, it seems wise to recommend some test of liver function as a routine procedure in this group of patients.

A decrease in plasma prothrombin is found early in impending liver failure. The Quick¹⁸ method of plasma-prothrombin determination is simply and easily performed and is relatively inexpensive. It is suggested that such prothrombin determinations be done every three days in seriously ill pa-

ients receiving sulfonamide therapy. In this way it should be possible to recognize patients in whom serious hepatitis is apt to develop before the symptoms have become clinically alarming.

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SIMULTANEOUS HYPERFU AND PARATHY

EDWARD S MILLER, M.D.[†] AND LIE

BOE

THE concurrence of hyperthyroidism and hyperparathyroidism is a clinical rarity; a patient with such a syndrome forms the basis of this report. She presented a confusing symptomatology, so that in retrospect it seems worth while to indicate the clues that could have led to a pre-operative diagnosis. Although such a combination is unusual, this case is by no means an isolated example.

CASE REPORT

M W, a 51 year-old, married housewife, was admitted to the Medical Service of the Peter Bent Brigham Hospital on November 4, 1941. She complained of weakness, abdominal distress and vomiting of 8 months' duration. The past history was of interest in that 10 years previously her physician had noted that her thyroid gland was enlarged. Four years previously she passed what was thought to be a renal calculus. She had no other urinary symptoms. One year prior to admission there occurred a 3-week episode of vomiting and abdominal pain, diagnosed as gall-bladder disease. From 16 months until 2 months before admission the patient took 1 tablet of thyroid each day. The basal metabolic rate was not determined. The

*From the Medical Service, Peter Bent Brigham Hospital.

†Formerly, medical house officer, Peter Bent Brigham Hospital.

The hemoglobin was 10.1 gm., and the blood smear was normal except for moderate variation in the size and shape of the red cells. Urinalysis was negative. The serum cholesterol was 181 mg. per 100 cc. The gastric contents contained free acid after histamine. The basal metabolic rates in a series of determinations were +36, +29, +23, +25 and +31 per cent. The decholin circulation time was 12 seconds. The heart and lungs were negative to x-ray examination, although the trachea was displaced to the left. The bony thorax was normal. A gastrointestinal series demonstrated no abnormalities. Prostigmine injection produced no change in muscular activity.

During the patient's stay on the Medical Service her temperature fluctuated each day, rising as high as 101°F. by rectum. The heart rate was usually between 120 and 150, even during sleep. She was hyperactive and retched frequently. She had been taking iodine during the month prior to admission, and this drug was continued. Myasthenia remained a prominent aspect of the symptomatology. There was no clinical improvement, and on November 17 the patient was transferred to the Surgical Service for thyroidectomy.

The following day operation was performed under novocain anesthesia. A rather large, vascular, hyperplastic thyroid gland was found, and a radical subtotal thyroidectomy was performed. In addition, there was a yellowish tumor at the lower pole of the left lobe, which had the gross appearance of a parathyroid gland. Venous blood was taken for chemical determinations, and the tumor was removed.

Significant blood studies were as follows:

TIME	CALCIUM mg./100 cc.	PHOSPHORUS mg./100 cc.	PHOSPHATASE Bod. units/100 cc.
At operation .	17.2	2.5	3.2
Postoperative day:			
2nd . . .	16.4	3.1	
4th . . .	11.4	1.0	
6th . . .	11.4		
9th . .		2.4	
14th .	7.6	2.2	
Normal	9-11	2.5-4.5	2-4

It is evident that during and immediately after operation this patient's serum calcium was considerably elevated whereas the phosphorus was decreased—findings that are typical of hyperparathyroidism. The normal phosphatase level was consistent with the paucity of bone changes.

The postoperative course was uneventful except for the development of mild tetany on the 7th day, controlled with calcium gluconate intravenously. Other x-ray studies at this time demonstrated a nonfunctioning gall bladder. Films of the long bones showed the bone detail and calcium content to be normal except for slight osteoporosis of the femurs. Skull films revealed a normal sella, with a mild degree of osteoporosis of the vault. Intravenous urograms were normal. Moderate hypochromic anemia persisted. Three weeks after operation the basal metabolic rate was -26 per cent. The patient returned home on a maintenance dose of viosterol and calcium gluconate.

The patient was seen again 4 months after operation, at which time she was in excellent health and had regained the 40 pounds previously lost. The only complaints were soreness of the shins and ankle edema, which appeared only with walking. These phenomena were attributed to the prolonged period of confinement to bed. The basal metabolic rate was -1 per cent, the serum calcium 10.2 mg. per 100 cc., the serum phosphorus 3.1 mg., the

phosphatase 1.1 Bodansky units, and the hemoglobin 14.9 gm.

Pathological report: The thyroid tissue when removed weighed 53 gm., was homogeneously pink, and showed a few small nodular areas. Histologic sections revealed closely spaced follicles, some of which were lined with low cuboidal cells and others with tall columnar cells (Fig. 1). The stroma was richly vascularized, and there were occasional collections of lymphoid tissue. The findings were typical of hyperplasia of the thyroid gland with iodine involution.

At the left lower pole of the thyroid gland was a parathyroid gland weighing 2.5 gm. Microscopic examination disclosed closely packed cells in cords, with occasional alveolar formations. The cells were polyhedral and small, and contained finely granular and slightly basophilic cytoplasm with round nuclei rich in chromatin (Fig. 2). Some of the alveolar formations were lined with these cells and contained small amounts of pinkish material. There were numerous eosinophils in the highly vascular stroma. The pathological diagnosis was adenoma of the parathyroid gland.¹

CASES IN THE LITERATURE

We were able to find in the literature 5 cases of this combination of hyperthyroidism and hyperparathyroidism. Meyer-Borstel's² patient had severe Graves's disease associated with generalized osteitis fibrosa cystica. This patient was seen in 1922, at a period when the association between the bone disease and hyperparathyroidism was not clearly defined. Consequently, when she underwent thyroidectomy a parathyroid tumor was neither searched for nor found. Ballin and Morse³ cited a case with symptoms of hyperthyroidism in which "a calcified adenomatous goiter" was removed. During the next few years the patient developed bone pains and decalcification, and this time a parathyroid adenoma was found at operation. Ball⁴ reported a case with an elevated basal metabolic rate and an increased serum calcium, in which the combined diagnosis was made clinically. At operation a "colloid and fetal adenoma" of the thyroid was found. Search for a parathyroid tumor was fruitless. The serum calcium remained elevated after operation. Hellström's patient⁵ had a basal metabolic rate of +50 per cent, a serum calcium of 14 mg. per 100 cc. and generalized osteitis fibrosa cystica. She was not subjected to operation. Noble and Borg⁶ reported a case that was confirmed at operation. Cooley's patient⁷ probably does not fall into this group, for although the basal metabolic rate was +23 per cent, there was a colloid goiter histologically.

DISCUSSION

Our patient's preoperative course was unusual in several respects, and was the subject of considerable discussion. She had taken a daily dose of thyroid for an extended period of time, but this

medication was stopped two months before entry. It was believed that her symptoms of thyrotoxicosis in this patient. Another confusing symptom was abdominal distress and tenderness. These prob-



FIGURE 1. Photograph of Section of Thyroid Gland, Showing Hyperplasia with Iodine Involution (eosin and methylene blue, 200 \times).

could not be attributed to this. There was a considerable degree of nausea, vomiting, weakness and lems were of course clarified by the finding of a parathyroid adenoma

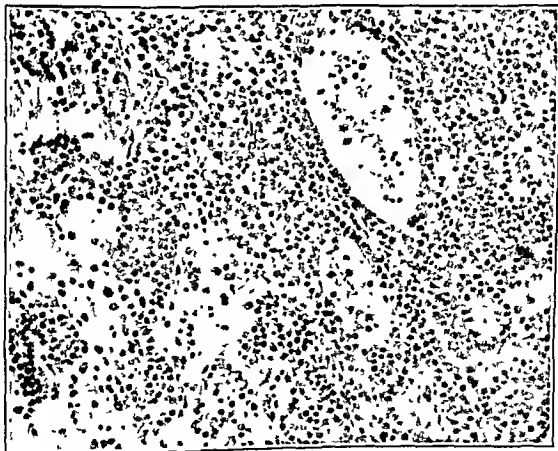


FIGURE 2. Photograph of Section of Parathyroid Adenoma (eosin and methylene blue, 200 \times).

anemia. These symptoms can occur in hyperthyroidism, but they are not commonly so severe as In Table I are listed the most frequent symptoms and signs characteristic of hyperfunction of the

thyroid and parathyroid glands, as well as those common to both.⁸⁻¹¹ It is evident from this table

TABLE 1. *Symptoms and Signs in Hyperfunction of the Thyroid and Parathyroid Glands.*

SYMPTOM OR SIGN	PRESENT IN CASE REPORTED
Common to hyperthyroidism and hyperparathyroidism:	
Mass in neck	+
Weight loss	+
Anorexia	+
Nausea and vomiting	+
Weakness and fatigue	+
Osteoporosis	.
Polyuria and polydipsia	
Increased urine calcium	
Increased serum phosphatase	-
Found particularly in hyperthyroidism	
Nervousness	+
Tremor	+
Tachycardia and palpitation	+
Eye signs	+
Thrill and bruit over gland	-
Perspiration and warmth	+
Pressure symptoms (cough and dyspnea)	+
Diarrhea	+
Oligomenorrhea or amenorrhea	+
Increased basal metabolic rate	+
Good appetite	
Found particularly in hyperparathyroidism.	
Metastatic calcification, especially renal stones	+
Abdominal distress and pain	+
Cold extremities	+
Hypochromic anemia	+
Increased serum calcium and decreased serum phosphorus	-
Ostitis fibrosa cystica, bone pains, bone tumors, fractures and deformities	
Renal insufficiency	
Bradycardia	
Constipation	

that there are striking and confusing clinical similarities. In the presence of thyrotoxicosis there are relatively few factors that lead one to suspect a superimposed hyperparathyroidism. These include

osteitis fibrosa cystica, metastatic calcification, marked hypochromic anemia and, of course, increased serum calcium. In the case under discussion, the significant clinical features that could have led to the proper diagnosis were a history of renal stone, abdominal distress, anemia, marked nausea and vomiting, and unusual asthenia.

One may speculate on a possible common etiologic factor in this syndrome. The obvious link that comes to mind is the pituitary gland. In this patient, however, there was no evidence of pituitary disease.

SUMMARY

A case of simultaneous hyperthyroidism and hyperparathyroidism is presented. Other case reports are reviewed.

The salient factors in diagnosis are summarized.

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COMPLETE SITUS INVERSUS

Report of a Case with Calcareous Aortic Stenosis and Cor Bovinum

JOSEPH G. PASTERNAK, PASSED ASSISTANT SURGEON, U.S.P.H.S.*

STATEN ISLAND, NEW YORK

ALTHOUGH congenital cardiac anomalies and defects have frequently been found associated with situs inversus,¹ reports of acquired cardiac lesions are rare. Owen² reported a case of mitral stenosis, and King³ one of syphilitic aortitis, aortic insufficiency, cardiac hypertrophy and myocarditis with a mural thrombus

heart. There was no history of rheumatic fever. An electrocardiogram was interpreted as showing dextrocardia. There was complete inversion of Lead I and transposition of Leads 2 and 3. The heart was compensated, only moderately enlarged, and showed no evidence of myocardial damage. From the age of 15, the patient had worked at laborious occupations, unrestrained. He stated that he had had a serious lung or heart ailment in 1907.



FIGURE 1 *Situs Inversus Totalis*
Note the greatly hypertrophied heart

The first case of complete situs inversus with calcareous aortic stenosis, cor bovinum and multiple pulmonary infarcts, is now reported.

CASE REPORT

A 43-year-old Swede entered the United States Marine Hospital on September 15, 1941, because of a cold and productive cough of 3 weeks duration. He had been treated in this hospital for gonorrheal urethritis in 1938. At that time a diagnosis of dextrocardia with aortic stenosis was made. The patient had no symptoms referable to the

heart. On admission he complained of shortness of breath on exertion, paroxysmal nocturnal dyspnea and swelling of the ankles. He had persistent dull pain in the right chest and a feeling of "rawness" behind the lower sternum.

On physical examination the patient was found to be in moderate distress in congestive heart failure and cyanotic. There was marked edema of the lower extremities. The pulse was 96, regular, small in volume and equal on both sides. The apex beat was in the right 6th inter-space at the anterior axillary line. There was a marked systolic thrill in the 2nd and 3rd intercostal spaces to the left of the sternum. In this area a loud, harsh systolic murmur was heard which was audible over the entire precordium and in the neck. The aortic second sound

*Director, Department of Pathology, United States Marine Hospital, Staten Island, New York.

was replaced by a short, faint diastolic murmur. The liver was palpably enlarged on the left side.

An electrocardiogram showed inversion of the P and QRS waves in Lead I and marked right-axis deviation. The T waves were upright in all leads. Comparison of this electrocardiogram with the one made 3 years previously disclosed evidence of left-ventricular strain in the new one. A roentgenogram of the chest gave the maximum heart measurements as 10.8 cm. to the right and 7 cm. to the left; the transverse diameter of the chest was 28.4 cm. A lateral view showed shadows suggestive of aortic calcification. Roentgenograms after a barium

scopic examination revealed scattered areas of interstitial fibrosis and foci of old myocardial scarring. The coronary arteries showed more or less diffuse fibrosis of their walls with occasional foci of atheroma and calcification in the intima. Multiple old and recent infarcts were present in all lobes of both lungs.

SUMMARY

Complete situs inversus associated with calcareous aortic stenosis, cor bovinum and multiple pulmonary infarcts is reported for the first time.



FIGURE 2. *Calcareous Lesion of the Aortic Valve.*

meal showed complete transposition of the gastrointestinal tract. The Wassermann and Kahn tests were negative.

The patient responded to treatment for 6 weeks and thereafter went downward. He died December 20.

Autopsy. There was complete situs inversus (Fig. 1). The heart weighed 810 gm. The aortic orifice was stenosed and deformed, and the cusps were fused and massively calcified (Fig. 2). The calcified ring measured 4 mm. in thickness. Microscopic examination showed the calcified cusps to consist of hyalinized scar tissue with more or less cartilaginous metaplasia and calcification. The myocardium was markedly hypertrophied. Micro-

The cardiac lesions were compatible with an old rheumatic infection.

I am indebted to Drs. G. A. Abbott and Henry I. Russek for the clinical data used in this report.

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MEDICAL PROGRESS

PATHOLOGY: DISEASES OF BONE

TRACY B MALLORY, MD*

BOSTON

TO MOST physicians the rarer diseases of bone with their multiple polysyllabic and still more confusing eponymic terminologies constitute the most perplexing field in medicine, a field so esoteric that it is apt to be relegated far back into the realms of the subconscious. This confusion, it must be admitted, is not unwarranted since there is justifiable suspicion that it afflicts the experts to an almost equal, albeit unadmitted, degree. In the last few years enough new observations have been placed on record to help in delineating these various entities to make a summary worth while at the present time.

HAND-SCHULLER-CHRISTIAN'S DISEASE, LETTERER-SIWE'S DISEASE AND EOSINOPHILIC GRANULOMA OF BONE

Hand-^{1 2} Schuller-^{3 4} Christian's⁵ disease, in its fully developed form as first described by Christian with the triad of multiple defects of cranial bones, exophthalmos and diabetes insipidus, has become a familiar picture, in the textbooks at least, though probably relatively few physicians have actually had a case under their own observation. That other cases lacking one or more features of the triad exist is less well known, and such cases are more likely to escape recognition and report. Yet Burger,⁶ in an assemblage of cases from the literature, found that 22 of 48 cases fell in this category. Also less generally realized is the possibility of other osseous localizations, in the pelvis, ribs, phalanges and even the long tubular bones, of lymph node and splenic involvement and, still more important, since they are life-endangering, of destructive lesions of the bone itself (Letterer⁷).

For somewhat over a decade, since the comprehensive studies of Rowland,⁸ Hand-Schuller-Christian's disease has been classified with the disturbances of lipid metabolism — Gaucher's disease with its storage of keratin, Niemann-Pick's disease with phosphatide abnormality and Hand-Schuller-Christian's disease as the corresponding disturbance of cholesterol metabolism. Significant reasons for questioning the correctness of this con-

venient schematization exist and have recently been re-emphasized (Letterer, Wallgren⁹ and Farber^{10 11}).

From the pathological point of view it is evident that Hand-Schuller-Christian's disease is not a simple so called "storage disease," like Niemann-Pick's or Gaucher's disease. It invariably shows the histological characteristics of a granulomatous process accompanied by significant grades of inflammatory reaction, both leukocytic and fibrotic. Yet cholesterol storage, which can readily be provoked by the feeding of cholesterol to rabbits, does not result in a granulomatous inflammatory reaction. Moreover, the spontaneous familial disease of man characterized by cutaneous xanthelasma, hypercholesteremia and extensive deposits of cholesterol and its esters in tendon sheaths and other tissues — familial xanthomatosis^{12 13} — is not associated with granulomatous reactions and never shows the destructive lesions of bone that characterize Hand-Schuller-Christian's disease. It is also noteworthy that no familial or even racial tendency has ever been noted in the latter, in contrast to the other storage diseases.

Cases of Hand-Schuller-Christian's disease do not ordinarily come to the attention of a physician in the early stages of their development. The bone lesions are usually so slow in their development and so painless that they remain unnoticed for a long period. When, however, the disease has been recognized at a comparatively early period or a fresh lesion is biopsied in a case of longer standing, it has been the usual experience that the granulomatous reaction is present but there is as yet little or no lipid deposit (Freund and Rippes¹⁴). Cholesterization occurs only with progression of the disease and is secondary, not primary (Letterer⁷).

As the significance of cholesterol has diminished in the conception of the pathogenesis of Hand-Schuller-Christian's disease, more attention has been devoted to the antecedent granulomatous reaction and new relations have become apparent. Wallgren,⁹ for instance, in an extremely lucid article argues that Letterer-Siwe's¹⁵ disease or leukemic reticulosis (Letterer¹⁶), or diffuse reticuloendotheliosis (Siwe¹⁷), or nonlipoid histiocytosis (Foot and Olcott¹⁸) is only a variant of the same pathologic process. Typical Letterer-Siwe's dis-

*Reprints of articles in this series are not available for distribution but the articles will be published in book form. The current volume is *Medical Progress Annals* Vol III 1942 (Springfield Ill no 3 Charles C Thomas Company 1942 \$5.00).

*Assistant professor of pathology Harvard Medical School director Department of Pathology and Bacteriology Massachusetts General Hospital

ease rarely occurs beyond two years of age and runs a rapidly and, it is at present believed, inevitably fatal course. It is characterized clinically by fever, skin rash, rapidly progressive anemia and purpura and histologically by marked proliferation of the so-called "reticuloendothelial" (monocytic and clasmatocytic) cells in many parts of the body, particularly the skin, the lymph nodes and the spleen. Occasionally the process simulates neoplasm so that it has been classified with the pseudo-leukemias; more often it presents an inflammatory, granulomatous character that suggests infection. Some of these cases show significant amounts of lipid storage in the proliferating cells. Certain cases, moreover, otherwise typical of Letterer-Siwe's disease, have shown focal destructive lesions of bone, with or without lipid deposits, quite indistinguishable from Hand-Schüller-Christian's disease (Schultz, Werbter and Puhl¹⁹ and Wallgren [Case 2]⁹). If the series of reported cases are listed in the order of their chronicity, as Wallgren has done, every grade of transition between the two diseases can be seen. In early infancy a malignant course is invariable, and the patient dies before complete development of the lesion, and before time has elapsed sufficient for secondary lipid degeneration. In later infancy greater chronicity is the rule and some of the features of Hand-Schüller-Christian's disease begin to make their appearance. From the age of two onward the disease is ordinarily chronic, lipoidal stages develop with considerable frequency, and by the age of three or four the typical picture of Hand-Schüller-Christian's disease is the rule.

A third condition, independently described as a new disease entity by Otani and Ehrlich²⁰ and by Lichtenstein and Jaffe²¹ as solitary or eosinophilic granuloma of bone, may well, in the opinion of Farber,^{10, 11} be still another variant of the same pathologic entity. The cases described by these two pairs of authors occurred for the most part in children in the later stages of childhood but also in adults, and were characterized by tumorlike destructive swellings of bone, usually single but occasionally multiple. Not infrequently the patients showed low-grade fever and leukocytosis, and occasionally blood smears disclosed significant grades of eosinophilia. Either excision of the lesion or x-ray treatment following biopsy was followed by rapid cure. Histologically the process is a granulomatous inflammatory lesion with marked accumulation of mononuclear phagocytes, often many foreign-body giant cells and variable numbers of eosinophils, sometimes tremendous. In one of Otani and Ehrlich's cases, however, eosinophils were entirely absent. It is interesting to note that the same histological picture was well described in a

beautifully illustrated paper by Fraser²² in 1935 as a variant of Hand-Schüller-Christian's disease.

Farber¹¹ has collected a group of 10 cases of granulomatous destructive lesions of bone. In this material he was able to find every grade of transition from typical Hand-Schüller-Christian's disease to the eosinophilic granuloma of Otani and Ehrlich and of Lichtenstein and Jaffe. Clinically typical Hand-Schüller-Christian's disease may show in various lesions xanthomatoid pictures with or without eosinophils, and eosinophilic granulomas without lipid degeneration. My own experience with 5 cases, only 2 of which have yet been published,^{23, 24} is entirely in accord with these findings. Among these cases was an example of clinically typical Hand-Schüller-Christian's disease in a child, in which a lymph-node biopsy yielded the typical picture of eosinophilic granuloma without lipid deposits; also there were 2 cases in adults with solitary lesions of the cranial bones, one with and one without eosinophils, but both showing extensive cholesterol deposits and the characteristic histologic picture of Hand-Schüller-Christian's disease.

One final variation in the picture remains to be mentioned. Farber points out that in certain cases in children the eosinophil proliferation may be so rapid that differentiation is incomplete and eosinophilic myelocytes may dominate the histologic reaction. The possibility of confusion with neoplastic processes of the myeloid series of cells is very great, and beyond question certain of these lesions have been classified as myelomas and myeloblastomas by competent observers.

Strongly suggestive evidence therefore lies at hand that all these various syndromes represent a single disease entity—rapidly fatal in the infantile forms, which have been described as Letterer-Siwe's disease and reticuloendotheliosis; chronic, but still of serious import because of the likelihood of cerebral and hypophyseal involvement, in early childhood (Hand-Schüller-Christian's disease); and comparatively benign in later childhood or in the adult, where the usual picture is that of eosinophilic granuloma. Proof of this identity must of course await the discovery of the etiology. Recent pathological studies point strongly away from a fundamental metabolic disorder and in the direction of a specific infectious agent.

OSTEITIS FIBROSA DISSEMINATA, POLYOSTOTIC FIBROUS DYSPLASIA, REGIONAL FIBROCYSTIC DISEASE AND ALBRIGHT'S DISEASE

Under the terms listed in the above heading and more than a score of other names, examples have been recorded of a confusing group of skeletal lesions for some of which fairly clear clinical and

pathologic pictures are beginning to emerge. The most extensive skeletal changes are usually found as part of a syndrome that includes changes in the skin and in the function of certain endocrine glands. The syndrome has been most clearly described by Albright and his numerous collaborators,^{25, 26} although individual case reports have been found dating back at least to von Recklinghausen. The essential features are as follows: multiple destructive lesions of bone simulating closely the generalized osteitis fibrosa of hyperparathyroidism and renal rickets but showing a distinct tendency to unilateral distribution; pigmented spots in the skin, also often restricted to one side of the body; and precocious puberty in female but not in male patients. An unusual feature of the precocious puberty associated with this syndrome, sharply separating it from other forms such as may occur with adrenal or ovarian tumors, is that there is no loss of fertility. Indeed one patient with this disease, a Peruvian girl, Lena Medina, won world-wide notoriety when she was delivered of a child at the age of five.²⁷

It is clear that the bone lesions are not due to abnormal parathyroid activity. Although the blood calcium and phosphatase may be moderately elevated in the active stages of the disease, the phosphorus is never depressed and there is no increased excretion of calcium in the urine. The uninvolved bones fail to show the generalized decalcification characteristic of hyperparathyroidism. Finally, under mistaken diagnosis, the parathyroid glands have several times been explored and on one occasion the removal of two normal glands was followed by unmistakable symptoms of tetany.²⁸

As in Hand-Schüller-Christian's disease, however, there is reason to doubt that all cases, or even, in the opinion of Lichtenstein and Jaffe,²⁹ any considerable proportion of them, present the complete triad of bone lesions, skin pigmentation and precocious puberty. Female patients with typical bone and skin lesions may not give a history of precocious puberty. Characteristic multiple bone lesions of unilateral distribution are found without skin pigmentation or endocrinopathy. Monomelic involvement—the restriction of lesions to the bones of a single extremity—has frequently been observed. Finally, single lesions of bone—so-called "osteitis fibrosa localisata"—are comparatively common which by x-ray and on gross and histologic examination of excised specimens are indistinguishable from individual lesions of the disseminate type.

From the clinical point of view, certain similarities between the localized and disseminate forms are apparent. The lesions usually appear in youth, commonly in later childhood or adolescence. Their development is evidently slow and often associated

with little pain. Consequently they may remain undiscovered for long periods of time until a pathologic fracture and consequent x-ray examination call attention to their presence. After a certain period they tend to become quiescent, although it is doubtful if they ever spontaneously heal and disappear. Little evidence exists, however, that the localized disease ever tends to become generalized. Both flat and tubular bones may be involved, and in the latter the epiphysis is almost always spared. Although the metaphysis is most frequently involved, even the midportion of the diaphysis may be the site of a lesion.

From the roentgenologic point of view the lesions closely simulate those of hyperparathyroidism, with the notable exception that the uninvolved bones are completely normal without evidence of generalized decalcification.^{27, 30} The process appears primarily destructive and usually expansile, with marked thinning of the cortex and no periosteal reaction unless complicated by fracture. Usually the density of the bone is considerably, though often irregularly, diminished and the picture frequently suggests cyst formation, an impression belied by the pathologic findings, which rarely show cyst formation of more than microscopic dimensions in the midst of solid tissue.

When one of these lesions is explored it is found to consist of fibrous tissue of variable density, which usually feels gritty. Microscopic examination proves this to be due to spicules of poorly formed and often imperfectly calcified membranous bone which, in the opinion of Lichtenstein,³¹ is formed by metaplasia from the fibrous tissue. In some cases islands of hyaline cartilage are present.

In the opinion of Lichtenstein and Jaffe²⁹ this histologic picture is sufficiently distinctive to be regarded as specific, even pathognomonic. If they are correct, another not uncommon condition must be brought into the fold. This is the tumor, or at least tumorlike condition, of the jaws that has been variously reported as ossifying fibroma and fibrous osteoma.³¹⁻³³ As Lichtenstein³¹ has pointed out, the histologic picture is identical with that of fibrous dysplasia. As in the latter disease the onset is in youth, usually in adolescence, and the outlook is favorable.

The majority of observers are as yet unprepared to accept the opinion of Lichtenstein and Jaffe that the histologic picture is pathognomonic, and point out that osteitis fibrosa is seen in hyperparathyroidism, in renal rickets, in some stages of Paget's disease and perhaps even in certain infectious lesions of bone. Lichtenstein and Jaffe, in contrast, assert that in most cases with a biopsy of adequate dimensions there are sufficient differences in the character of the bone formation and bone destruction, as well as in the fibrous tissue substrate to

make distinction readily possible. The wealth of material provided by the clinic of the Hospital for Bone and Joint Diseases is so great, and the authors have evidently studied it with such thoroughness and care, that their opinions deserve the most serious consideration.

In another direction also the specificity of the lesion they have described has been challenged. This is shown by the frequent use of the term "fibrocystic disease,"³⁵ under which solid and cystic lesions have been indiscriminately grouped. Jaffe and Lichtenstein,³⁶ again, have given special consideration to cystic disease of the bone. Under the name of "solid unicameral bone cyst" they describe their experience with 19 cases of true bone cyst. These are solitary, fluid-filled lesions of long tubular bones, most often of the humerus and femur. The surrounding cortex is expanded and thinned. The lining is ordinary fibrous tissue. They arise in youth, particularly in adolescence. The process starts in apposition with an epiphyseal line, but if untreated may extend to involve the major portion of the shaft. With growth, normal bone may be laid down between the cyst and the epiphyseal line so that the lesions may appear to migrate toward the center of the shaft.

Whatever the ultimate verdict may be regarding the specificity of fibrous dysplasia and the relation of the localized and disseminate forms, this group of lesions well warrants increased attention from clinician and pathologist alike. The former should be on his guard to pick up the localized form of the disease in any patient with a history of repeated fractures, particularly those of the same bone. He must likewise guard by careful blood-chemical determinations against confusing the generalized disease with hyperparathyroidism and subjecting his patient to a needless cervical operation. For the pathologist the greatest danger in this group of lesions lies in the possibility of confusion with malignant neoplasms, particularly in cases complicated by fracture and atypical reparative processes. The development of sarcoma in such a lesion has yet to be reported. Extreme caution should be observed in the face of scanty and possibly inadequate biopsies, and the precaution of checking with expert radiologic opinion should never be omitted.

In the realm of therapy little new has been offered. Nothing whatever is known that will affect the progress of the disseminate disease. Individual lesions in important bones may be treated by curettage, packing with bone chips or the use of solid bone grafts. Recurrence, however, is not infrequent. Radiation therapy is entirely ineffective.

The etiology of this entire group of lesions remains completely mysterious. Their localized character and the well-marked tendency to uni-

lateral distribution rule out a hormonal basis, except, perhaps, as a contributing factor. A congenital abnormality of bone development, possibly mediated in some way through the nervous system, seems the best solution as yet offered. Bremer³⁷ has suggested an interesting hypothesis based on analogy with the development of the air sac in the humerus of chickens. This has been shown to be dependent on the action of estrin, and the bone is hollowed out immediately below the epiphyseal line by an osteoclastic osteitis fibrosa very similar to the lesion of hyperparathyroidism. The development of lesions during adolescence and their association in certain cases with precocious puberty would fit such a theory. Although of great interest, it is manifest that any such hormonal influence could explain only a part of the picture.

OSTEOID OSTEOMA

Under this title Jaffe^{38, 39} and Lichtenstein⁴⁰ have described what appears to be a new disease entity probably clinically misinterpreted heretofore as sclerosing, nonsuppurative osteomyelitis or cortical bone abscess. The lesion proper consists of a rather small spherical nodule of vascular mesenchymal tissue closely packed with osteoblasts, which quickly lay down intercellular osteoid tissue that is slow to calcify. Eventually, however, calcification and even hypercalcification beyond the density of normal cortical bone occur. Equally characteristic of the process is the stimulation of reactive proliferation in the surrounding bone, so that the small primary focus is more or less encapsulated by a comparatively large mass of newly formed and very dense cortical bone. The lesion has been seen in nearly all the bones of the extremities and also in the vertebrae, but has not as yet been observed in the skull, pelvis or ribs. It develops in youth, commonly between the ages of ten and twenty-five, and appears to be more frequent in males than in females. Almost invariably, the principal symptom is pain, which is extremely persistent but generally not of great intensity, since several months commonly elapse before the patient comes under surgical observation. Local examination usually reveals tenderness and slight swelling. There are no systemic evidences of infection, such as fever and leukocytosis, and there is seldom any convincing history of trauma.

The roentgenographic picture constitutes the most valuable single diagnostic guide but is frequently misinterpreted. In the early stages of the disease the osteoid osteoma proper is indicated by a round or oval focus, 0.5 to 1.0 cm. in diameter, of relative radiolucency. This is surrounded by a perifocal reaction of newly formed and very dense bone, which may be limited to a relatively

narrow ring or may spread for several centimeters about the lesion. Later in its evolution, when the osteoid osteoma tends to become calcified, it no longer appears as an area of uniform rarefaction but begins to show focal and later complete opacity. This is the stage at which it is very apt to be misinterpreted as a sequestrum. To bring out the details of the lesion overexposed plates are frequently necessary.

Treatment in all the cases yet reported has consisted in excision of the osteoid focus and of the overlying reactive bone. This has been followed by immediate relief of pain, and no recurrences are on record.

The etiology remains mysterious. Infection seems to be ruled out by the absence of systemic reaction, by the complete absence of histologic evidence of inflammation in the lesion itself and by the negative results of all bacteriologic investigations. The pathologic picture in no way resembles that of aseptic necrosis of bone, and there is rarely a convincing history of trauma. Jaffe^{38, 39} strongly supports a neoplastic origin. Against this must be cited the limited growth capacity of the primary osteoid focus, which regardless of duration rarely exceeds 1.5 cm. in diameter.

CAISSON DISEASE OF BONE

Aseptic necrosis of bone of infarctlike character without demonstrable cause for vascular occlusion has long been recognized as the anatomic basis of Legg-Perthes's, Osgood-Schlatter's, Koehler's and Kienböck's diseases. Kahlstrom, Burton and Phemister⁴¹ have recently reported 4 cases of extensive aseptic necrosis, involving numerous bones, in victims of caisson disease. The lesions are limited to the long tubular bones of the extremities. When the lesions were situated in the epiphyses and bordered on joints, collapse of weight-bearing portions usually occurred, overlying articular cartilage broke down, osteocartilaginous loose bodies often appeared, and extensive arthritis deformans developed. When the necrotic bone focus was not in approximation with a joint surface, collapse did not occur and attempts at organization were apparent, but only in the smaller foci was this ever complete. In the larger areas the necrotic focus persisted indefinitely (up to thirty-five years in one case) with only a narrow shell of densely calcified reactive bone at its periphery. The pathogenesis is discussed by these authors, and two alternative theories are contrasted. The first is intravascular air embolism. Against this was the absence in one autopsied case of any infarcts of internal organs despite multiple foci in the bones. Secondly, the attempt to reproduce the picture in animals by air embolism was unsuccessful. The alternative concept is the extravascular liberation of gas

bubbles in such numbers that circulation is arrested by extravascular tension. In favor of this theory is the restriction of lesions to the tubular bones, which contain fatty rather than hematopoietic marrow. It has been shown that fat tissue absorbs four to five times as much nitrogen under conditions of increased pressure as do other kinds of tissue. Therefore far more gas is available for release, and its sudden liberation within a non-expandable bony shell may adequately explain the development of the lesion.

It should be pointed out, however, that indistinguishable multiple lesions of bone have been observed by Chandler⁴² and more recently by Kahlstrom, Burton and Phemister⁴³ in patients who have never been exposed to high atmospheric pressures. The general pathogenesis of aseptic necrosis of bone therefore remains as heretofore an unsolved problem.

MELORHEOSTOSIS

This formidable name is derived from two Greek words meaning "limb" and "I flow." It refers to the extraordinary appearance of affected bones on x-ray examination. This was originally described by Léri and Joanny⁴⁴ as *coulée de bougie*, because of its resemblance to the incrustations of molten wax along the side of a candle. Franklin and Matheson⁴⁵ have reported another case and reviewed the literature, which now includes 39 cases.

The affected bones are markedly thickened by irregular cortical overgrowths which project chiefly outward, although some encroachment on the marrow cavity may also occur. Usually multiple bones of a single extremity are involved and there is no greater frequency in the upper than in the lower limbs. Bilateral involvement has been observed in 5 cases, whereas the case of Franklin and Matheson showed almost perfect unilateral distribution, including the parietal and mandibular bones, the innominate bone and two ribs, as well as the tubular bones of the extremities, a more frequent site. Nine vertebrae likewise showed changes limited to the right side of the neural arch, but a single vertebra, the fifth lumbar, showed bilateral involvement. Histologic examination showed distortion and compression of the bone pattern with increased osseous density and a proportionate decrease in the number and size of the Haversian canals. There was evident predominance of bone formation over destruction, and although rare osteoblasts were identified, no osteoclasts were seen. The marrow was usually fibrous.

The symptoms of this unusual disease are vague and may be little more than the discomfort of the greatly increased weight of an affected limb. On examination, asymmetry of the face or limbs is usually apparent and nodular bony thickening may

be felt. The x-ray appearance of the *coulée de bougie* is pathognomonic.

ALBERS-SCHÖNBERG DISEASE, MARBLE BONES OR OSTEOPETROSIS

In this disease, which usually makes itself apparent in early childhood, the bones are of unusual density as judged by x-ray examination but of abnormal fragility from the clinical point of view, since they are prone to sustain repeated fractures from mild trauma. The underlying defect appears to be an inability to resorb bone, so that when new bone is laid down during growth the old bone is not removed. This may lead to pinching of nerves at their points of exit from the skull, and van Creveld and Heybroek⁴⁶ report blindness due to optic atrophy as the first symptom in a child. When the normal bone markings are not completely obliterated it is not unusual to see in x-ray films of the extremities transverse lines of increased density, which parallel the epiphyseal line. These are similar to the lines that can be produced experimentally by the intermittent feeding of phosphorus. Van Creveld and Heybroek made the interesting observation that these lines were laid down seasonally, the maximal density occurring in the autumn. With the failure of bone resorption, medullary cavities may fail to develop normally, leading to a myelophthitic anemia. The spleen and liver may be enlarged by compensatory myelopoiesis, and primitive cells of both the erythroid and myeloid series may be found in the peripheral blood. In certain cases the hematologic abnormalities completely dominate the clinical picture.

Metabolic studies in the hands of Kramer, Yuska and Steiner⁴⁷ showed normal levels in the blood for calcium, magnesium, phosphorus and phosphate. Chemical examination of the bone showed hypermineralization and an increase in the carbonate content. Further studies are, however, desirable since their case was complicated by moderately severe rickets.

The etiology of the disease is completely mysterious. The condition is evidently congenital and has been noted at birth. Drukker⁴⁸ in a survey of 121 cases found a familial incidence in 40 per cent.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28511

PRESENTATION OF CASE

First admission. A sixty-five-year-old physician was admitted because of a sense of oppression in the chest and "wheezing" at night.

Fourteen years prior to admission he was accidentally found to have a blood pressure of 200 systolic, 130 diastolic, and auricular premature beats. Accordingly he gave up smoking and took potassium sulfocyanate, $1\frac{1}{2}$ gr. three times a day every other month. Two years later the blood pressure was 190 systolic, 100 diastolic.

Eleven years previously, after working particularly hard, he noted a slight amount of dizziness, occasional episodes of ringing in the ears and subcutaneous hemorrhage of the left arm. Physical examination revealed subconjunctival hemorrhage of the left eye. The heart was enlarged, the apex being 10 cm. to the left of the midsternal line in the fifth intercostal space. The heart sounds were of good quality, and a harsh systolic murmur was audible at the apex and in the aortic area; no diastolic murmurs were heard. The pulse was irregular, owing to the presence of many premature beats, and the blood pressure was found to be 195 systolic, 115 diastolic. Fluoroscopic examination revealed a slight amount of cardiac enlargement and a marked tortuosity of the aorta, with a prominent knob. The patient was advised to limit his activities further, and to continue the potassium sulfocyanate medication as previously taken.

Four months before entry he noted a sense of dizziness and mild headache; at times he felt sluggish. He occasionally had to rest because of a feeling of mild chest oppression and an occasionally associated feeling of breathlessness. At that time he was taking aminophyllin, 3 gr. three times a day. Physical examination was unchanged except that the blood pressure was 230 systolic, 130 diastolic. The fluoroscopic examination was repeated and revealed a large left ventricle and a dense aorta; the lung shadows were normal. An electrocardiogram showed a normal rhythm of 75, moderate left-axis deviation and a slight diphasic T_1 .

Six weeks prior to entering the hospital he developed a mild "nasal" infection, which persisted

to the time of admission without variation in degree, accompanied by occasional slight elevation of temperature. One week before entry the feeling of chest oppression became more severe, exertional dyspnea developed and the patient felt "wheezy" at night.

Physical examination revealed a well-developed and well-nourished man in mild respiratory distress suffering with a mild upper respiratory infection. Examination of the heart showed the maximum apical impulse to be 11 cm. to the left of the midsternal line in the fifth intercostal space. The heart sounds were regular and of fair quality. At the base of the heart over the aortic area a moderately loud, slightly harsh systolic murmur was audible. To the left of the lower sternum a very soft blowing diastolic murmur was heard. At the apex of the heart a moderately loud slightly coarse systolic murmur and a diastolic third heart sound were heard, and these carried toward the lung base. Rales were audible at both lung bases posteriorly. The abdomen was flat and soft, and the lower edge of the liver, which was tender, was felt two fingerbreadths below the costal margin. No other abdominal masses were felt. There was no ankle edema.

The blood pressure was 200 systolic, 110 diastolic. The temperature was 99°F. , the pulse 78, and the respirations 20.

The examination of the blood revealed a hemoglobin of 12.4 gm. and a white-cell count of 5100 with 82 per cent polymorphonuclears, 12 per cent lymphocytes and 6 per cent monocytes. The blood Hinton test was negative. The non-protein nitrogen was 28 mg. per 100 cc. The urine had a specific gravity of 1.010, was acid in reaction and gave a $+$ test for albumin; the sediment contained a rare hyalin cast, 4 red cells and 1 white cell per high-power field. An electrocardiogram showed a normal sinus rhythm, with a rate of 60. T_1 and T_2 were inverted and sagging; T_4 was rather sharply inverted; and there was a moderate amount of left-axis deviation. An x-ray film of the chest demonstrated that the heart lay horizontally in the chest and that there was considerable enlargement of the left ventricle. The curve of the ventricle was prominent and the apex was blunted. The aorta was tortuous and prominent in the region of the knob and showed some calcification in its walls. There was also a slight bulge of aorta near the root. The lung fields were clear.

Three days after admission the patient noticed a slight amount of blood on his pajamas. This was attributed to congestion of a hyperplastic prostatic

After ten days the patient improved with and digitalis. His apparent upper-respiratory infection subsided, and he was ab-

get about satisfactorily without great discomfort. He left the hospital in the late afternoon.

Second admission (12 hours later). The patient returned to the hospital because of midepigastria discomfort, nausea and vomiting which had developed a few hours after a rather heavy supper. There was no substernal or back pain. The patient was obviously uncomfortable and was sweating. The examination of the heart revealed good heart sounds, a regular rhythm and murmurs as previously noted. Good vessel pulsations were felt in the legs. The lungs were normal. There was tenderness and some spasm over the entire abdomen, most marked on the right side, opposite and above the umbilicus. The tenderness was less striking in the right lower quadrant. The liver did not appear to be enlarged. There was questionable tenderness over the gall bladder. The peristaltic sounds at times seemed diminished. The rectal examination was negative except for slight enlargement of the prostate.

The blood pressure was unchanged, 200 systolic, 110 diastolic. The temperature was 99°F., the pulse 50, and the respirations 25.

The white-cell count was 20,000. The urine examination was negative except that the sediment contained 3 white cells per high-power field. An electrocardiogram was similar to the previous ones.

The patient was operated on two hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. T. D. JONES: The initial complaint suggests that the patient had coronary disease and a decrease in his cardiac reserve. One soon learns that he had persistent hypertension, the pressure remaining elevated at every determination over a period of fourteen years. There is little evidence that potassium sulfocyanate had any ameliorating effect. Dizziness, headaches, and ringing in the ears may be taken as a part of his hypertensive syndrome. Broken conjunctival blood vessels also occur in hypertensive patients.

Although the stature of the patient is not described, it is assumed that he was of average size. As would be expected, the heart was distinctly enlarged, and there was left-axis deviation by electrocardiogram. Initial fluoroscopy verified the clinical impression of hypertensive heart disease in a patient with definite arteriosclerosis, at least of the thoracic aorta. The murmurs described are not especially unusual in a patient with hypertension and arteriosclerosis. In a patient with these findings, a sense of oppression in the chest warrants a diagnosis of angina pectoris — and a consideration of the presence of coronary sclerosis. This was considered to exist, since he was given anti-anginal drugs. There is no definite indica-

tion that it was beneficial. Breathlessness was probably associated with the decrease in cardiac reserve.

For a few months prior to admission and especially for the preceding six weeks, there was an apparent increase in symptoms. On admission there was evidence of mild congestive heart failure, along with an increase in the feeling of chest oppression. This failure may have been precipitated by the recent mild respiratory infection that was thought to have persisted to the time of admission. The exact nature of the respiratory infection is impossible to determine in retrospect.

Failure was indicated by respiratory distress, slight enlargement of the liver, rales in the lung bases, and concomitant urinary changes. There was an obvious increase in the severity of the heart disease over previous examinations as indicated by the heart size. This is not surprising in view of the persistent hypertension and the story of slowly diminishing cardiac reserve. It is rather surprising that there was no evidence of actual renal disease after so many years of hypertension.

The murmurs are distinctly in keeping with the hypertensive and arteriosclerotic process and need not raise the question of rheumatic valvular disease. There was no evidence of aortic stenosis; syphilitic aortic disease seems unlikely in view of his age, the negative Hinton test, the absence of a syphilitic history and the prolonged period of symptomatology. A diastolic murmur resulting from syphilitic aortitis usually develops prior to symptoms, rather than after a long period of decreased cardiac reserve resulting from this condition.

The electrocardiograph was not too helpful. The changes raise the question of a previous slow occlusion of the coronary vessels. This suggestion must remain as a possibility despite no history of an acute coronary episode. The sharply inverted T₁ is suggestive, and certainly corroborates the impression of extensive heart disease.

The x-ray findings reiterate the question of the presence of sclerotic changes, at least in the ascending aorta. In view of the terminal episode the question naturally arises whether or not the arteriosclerotic process was more progressive than was apparent.

The question of finding blood on the patient's pajamas is confusing and does not help clarify the underlying process. As reported it is impossible to connect it directly with the patient's illness.

The second and final admission, twelve hours after hospital discharge, seems unquestionably a problem of an acute abdominal condition. In view of the previous history and findings, one would naturally expect the episode to be related to the hypertensive and arteriosclerotic syndrome, espe-

cially the latter. The acute symptoms began three or four hours prior to readmission to the hospital, and evidently were not too severe, otherwise immediate surgical intervention would have ensued. It would be helpful to know what happened to the blood pressure during this period, as it is distinctly lowered as the result of appreciable hemorrhage, of dissection of an arterial aneurysm and of acute coronary closure. So far as I am aware, it may or may not be lowered in mesenteric thrombosis. However, on admission the pressure was very near its previous high level.

Apparently there was no chest pain to suggest acute coronary closure, nor was shock so severe as one might expect in extensive hemorrhage or extensive aneurysmal dissection. Also against the latter is any indication of direction of dissection, usually suggested by the radiation of pain. It hence seems more likely that thrombosis or infarction of the mesenteric vessels comes nearer satisfying the general features presented by the abdominal emergency. Mesenteric thrombosis therefore is my preoperative diagnosis. This would not be too unusual in a person with long-standing hypertensive heart disease and coronary sclerosis, with some question of previous coronary closure. It seems likely that arteriosclerosis was the fundamental basis for the difficulty.

DR. PAUL D. WHITE: I saw this man in 1931 on two occasions because of his hypertension. He was apparently symptom-free at the time. He did not have an aortic diastolic murmur but only an aortic systolic murmur, which, because of his hypertension, I was inclined to think was not due to valvular disease. Dr. Edward Bland later raised the question whether the aortic systolic and diastolic murmurs were of rheumatic origin. He simply raised that question, but it is unlikely that at this patient's age there had occurred sufficient additional rheumatic disease to produce an aortic diastolic murmur.

A PHYSICIAN: In the presence of extensive calcareous valvular disease, could there be some degree of regurgitation?

DR. WHITE: I think that is more of a possibility here than rheumatic involvement, if there is any valvular disease at all.

A PHYSICIAN: Is not the story different from that of aortic stenosis of significant degree? Would you not expect him to have died sooner?

DR. WHITE: No. A good many patients do have acute failure,—left ventricular failure,—but not until ten or more years after the accidental finding of a murmur undoubtedly due to aortic stenosis. They can even live some years after the heart failure starts, despite a high degree of aortic stenosis.

DR. JONES: Can such a systemic pressure be sustained with aortic stenosis?

DR. WHITE: Yes, it can be done. I have seen a number of such cases.

DR. ERNEST M. DALAND: If you could have seen this patient yourself it would have been obvious that he had an acute abdominal condition with his maximum tenderness and spasm in the right upper quadrant, just above the umbilicus. There was questionable tenderness over the gall bladder, but he gave no history of previous gall-bladder disease or ulcer. Although he had a good deal of rigidity in the right upper quadrant, he did not have a board-like belly and a perforated ulcer was ruled out on that basis. He did not have enough localized tenderness over the gall bladder to make a diagnosis of acute cholecystitis. The possibility of appendicitis was considered. It seemed as if his acute abdominal condition must have had some relation to the previous illness, and so the diagnosis of mesenteric thrombosis was thought most likely. Under general anesthesia the abdomen was opened through a rather high midline incision. We found the appendix and gall bladder free of disease, and the liver was normal. The chief finding was a large retroperitoneal hematoma. This was below the level of the pancreas, at the root of the mesentery of the small bowel. It looked somewhat like an acute hemorrhagic pancreatitis except that there was no fat necrosis and we were able to palpate the pancreas separately from the mass. The mass was 8 to 10 cm. in diameter. The intestines showed good color, and no mesenteric thrombosis was found. We could not feel any aneurysm, and no further exploration was made. The postoperative diagnosis was retroperitoneal hemorrhage. The patient made a good recovery from operation. At the end of the operation his systolic blood pressure was down to about 100, but during the next few hours it returned to 200 and he felt quite well during the remainder of the day. He asked what the operative findings were and discussed the diagnosis quite intelligently. About four o'clock the next morning, about twenty-four hours after the operation, he suddenly went into collapse and was dead in a minute or two.

DR. TRACY B. MALLORY: At operation, a large retroperitoneal hematoma was found, source not determined. Does anyone care to speculate any further on the diagnostic possibilities?

DR. JONES: I presume he had an aneurysm that ruptured into a closed space. That changes the diagnosis from probable mesenteric thrombosis to a dissecting type of lesion.

DR. WHITE: Do you think it was necessarily a dissecting aneurysm? Could it have been hem-

orrhage from a saccular arteriosclerotic aneurysm of the abdominal aorta?

CLINICAL DIAGNOSIS

Mesenteric thrombosis.

DR. JONES'S DIAGNOSES

Hypertensive heart disease.

Coronary sclerosis.

Mesenteric thrombosis.

ANATOMICAL DIAGNOSES

Acute hemorrhagic pancreatitis with fat necrosis.

Retroperitoneal hematoma.

Slight hemoperitoneum.

Cardiac hypertrophy.

Arteriosclerosis: marked, aortic; moderate, pulmonary and coronary.

Nephritis, vascular, chronic.

Pulmonary edema.

Operative wound: exploratory laparotomy.

PATHOLOGICAL DISCUSSION

DR. MALLORY: We had considerable difficulty at the time of autopsy in determining the cause of the hemorrhage. The great bulk of the hematoma lay in the mesentery, which had been dissected into two leaves by the blood. Tracing this back we eventually tracked it down to the posterior surface of the head of the pancreas, where we found numerous areas of fat necrosis. At this point there was characteristic acute hemorrhagic pancreatitis, so-called "pancreatic apoplexy." A peculiar feature was that the blood instead of dissecting profusely through the pancreas had dissected largely into the root of the mesentery. The pancreatitis was limited to the posterior portion of the head of the pancreas. The body and tail were normal. It would not have been possible to recognize it at the time of operation because it was not until we approached the organs from behind that we found it ourselves.

The other findings were a markedly hypertrophied heart, weighing 550 gm. The coronary arteries were large and capacious with some arteriosclerotic plaques but no occlusion at any point, and the myocardium showed no areas of infarction. The aortic valve was entirely negative. There was no calcification, no stenosis or no regurgitation. The kidneys showed the characteristic nephrosclerosis to be expected in long-standing hypertension.

DR. WHITE: There are two things I should like to emphasize with respect to this case. First, there can be long-standing aortic systolic murmurs and even aortic diastolic murmurs without valvular disease.

Second, the electrocardiogram of a large hypertensive heart can closely resemble that of coronary heart disease.

DR. MALLORY: The ascending aorta was markedly sclerotic. So far as thrombosis is concerned there was no gross calcification but a little dilatation, and the aortic ring itself was of normal measurement.

DR. DALAND: Do you not think it surprising that no more was found in the pancreas at the end of thirty hours?

DR. MALLORY: It is very unusual.

CASE 28512

PRESENTATION OF CASE

First admission. This forty-four-year-old man was admitted because of a persistent cough.

One year prior to admission the patient developed a cough, which at times was productive of a slight amount of gray-white sputum. When he coughed he occasionally had substernal pain, but this was never severe. Four months before entry the cough increased and a greater amount of sputum was raised; this was thick and yellow but did not have an odor and never contained blood. At that time both ankles became swollen and stiff. His physician said that the edema was not of a "pitting type" and that the urine was normal. Despite the medication provided the cough was unimproved. The leg edema gradually increased to the knees, the ankle stiffness became more marked, and the knees became stiff, swollen, painful and slightly red. He also developed exertional dyspnea. During the entire period the cough became progressively worse.

One week before admission an electrocardiogram was said to have been normal. A chest roentgenogram disclosed some cloudiness in the lower left lung, but no diagnosis was made. A single sputum was negative for acid-fast bacilli. He was treated with "wheat-germ oil" injections, and two days later the joint pain and most of the leg swelling disappeared. During the week prior to admission he raised one fourth of a cup of sputum each day, which was very thick and had developed a foul odor. During the six months prior to entry he had lost 27 pounds.

The patient's mother died of "carcinoma of the throat," and his father died of heart trouble. The past history was noncontributory.

Physical examination revealed a prematurely gray man who was hoarse and who coughed frequently making him uncomfortable because of the associated chest pain. The heart was percussed 10 cm. to the left of the midsternal line. The heart sounds were of good quality, and no murmurs

were heard. There was decreased expansion of the left chest, with dullness over the upper left chest anteriorly and increased breath and voice sounds in this area. Scattered fine rales were audible at the left apex, and a friction rub was heard in the left midaxillary line. Examination of the abdomen was negative. There was swelling with some pitting edema of both lower legs. The ankles were slightly swollen but were not warm, red or tender. There was marked clubbing of the fingers and toes.

The blood pressure was 120 systolic, 70 diastolic. The temperature was 101°F, the pulse 95, and the respirations 30. The temperature and pulse continued to rise each evening.

Examination of the blood revealed a hemoglobin of 91 gm, a white-cell count of 20,800 with 88 per cent polymorphonuclears. The urine repeatedly was acid in reaction, had a specific gravity of 1.028 and gave a + test for albumin; the sediment contained 7 red cells and occasional white cells and epithelial cells per high power field. The blood Hinton test was negative. The blood protein was 5.9 gm per 100 cc, with 2.8 gm albumin and 3.1 gm globulin, making the albumin globulin ratio 0.9. The sputum examination was negative for acid fast bacilli on two occasions. A chest roentgenogram showed diffuse hazy density of the entire left lung field, and within this area there was a fairly sharply defined rounded mass lying posteriorly against the ribs and extending from the fourth to the eighth rib. There are multiple areas of rarefaction within this mass, and there were similar areas of rarefaction anterior to it in the right upper lobe. The mediastinum was displaced to the left. The left side of the diaphragm was high, and the left costophrenic angle was obliterated. There was no evidence of disease in the right lung, and the visible ribs and vertebrae showed no evidence of metastases.

On the third day after admission the patient was bronchoscoped. There was no widening of the lumen or fixation of the carina. At a point in the left bronchial tree about 5 or 6 cm below the carina the left main bronchus became narrowed and presented an irregular granular appearance on the lateral as well as the medial aspect. The left upper lobe orifice was not seen. Foul bloody secretion was aspirated, and several biopsy specimens were taken, which were reported as showing acute and chronic inflammation. On the ninth hospital day a left upper lobe abscess was drained posteriorly by resecting segments of the fifth, sixth and seventh ribs. The abscess was described as immature. It contained a moderate amount of gangrenous lung and small amounts of pus. It was traversed by several septa. Sulfanilamide pow-

der was implanted locally. A pleural biopsy was reported as showing acute and chronic pleuritis. The culture of the pus demonstrated a few alpha hemolytic streptococci and a moderate growth of nonhemolytic streptococci. After operation, the patient improved and the temperature and pulse returned to normal. He was discharged on the thirty-third day after admission.

Second admission (one month later). The patient was readmitted for study of the persistent ankle edema. After discharge there was little drainage from the chest. One week before entry the cough was slightly increased but little sputum was raised. Since the previous admission he had suffered with a great deal of exertional dyspnea but at no time was he orthopneic.

On examination the patient was plethoric and puffy faced, and coughed frequently. The neck veins were not distended. The trachea was slightly deviated to the left. The heart was percussed 8 cm to the left of the midclavicular line. The sounds were regular and of good quality. There seemed to be a split second sound audible at the apex. No murmurs were audible. There was a large cavity in the left posterior chest, from which a small amount of foul pus drained. Bronchial whistling was audible over this area. The left chest was dull on percussion. The abdomen was held tensely, however, no fluid was found and no masses were definitely felt. There were dilated veins in the lower abdominal wall. Clubbing of the fingers and toes was again noted. There was no evidence of phlebitis.

The urine and blood examinations were similar to those noted during the previous admission. The nonprotein nitrogen was 14 mg per 100 cc, the chloride 98.8 milliequiv per liter, and the protein 5.5 gm per 100 cc, with an albumin of 3.0 gm and a globulin of 2.5 gm, giving an albumin globulin ratio of 1.2. An electrocardiogram showed a normal sinus rhythm with a rate of 90. The PR interval was 0.16 second, T₁ was flat, and T₂, T₃ and T₄ were upright. The Congo-red test showed 100 per cent retention of the dye in the serum after one hour.

He was treated with a course of sulfathiazole, totaling 12 gm in four days, and was discharged unimproved nine days after admission.

Third admission (two months later). The patient was readmitted because of painful swelling and stiffness of the knees and ankles, which developed soon after leaving the hospital. The pain was dull and occurred intermittently each day, being worse in the morning, but at no time was it severe. The joints were not red or warm. During the three weeks prior to admission the pa-

tient had gained 10 pounds. The chronic cough had persisted, and occasionally there was blood streaking of the sputum. While at home he took sulfathiazole, which was later changed to sulfadiazine because of nausea, "dizziness" and the development of a rash on the face. He had nocturia, one or two times, and occasional urgency. He had not had any fever or rise of blood pressure.

Physical examination was similar to that already noted except that there was swelling of the ankles without redness, tenderness or pitting edema. There was no pain or limitation of leg-joint motion.

Examination of the blood revealed a hemoglobin of 10.7 gm. and a white-cell count of 20,300 with 64 per cent polymorphonuclears. In the smear the red cells appeared normal, and the platelets were slightly increased. The nonprotein nitrogen was 30 mg., and the protein 7.2 gm. per 100 cc. No acid-fast organisms were found in the sputum. The urine had a specific gravity of 1.010 and gave a $+$ test for albumin; the sediment contained 15 white cells, a rare red cell and 3 epithelial cells per high-power field; the pH was alkaline on three occasions and acid on two. A phenolsulfonephthalein test showed 17, 8, 12 and 15 per cent excretion of the dye in a quarter, a half, one and two hours respectively. A chest film showed little change in appearance since the last entry. The greater portion of the left upper lobe was honeycombed in appearance, showing numerous small cavities. The large abscess cavity was no longer definitely visible. The fluid in the left base had cleared. There was some inspiratory shift to the left, and the mediastinum was displaced to this side. The right lung field remained clear.

The patient was treated with 4 gm. of sulfadiazine and discharged unimproved on the third day after admission.

Fourth admission (two months later). The patient was readmitted for left pneumonectomy. Since discharge he had gained weight but continued to have cough and hemoptysis. He became dyspneic on climbing a flight of stairs. Ankle edema had not been severe.

Physical examination was similar to that of previous admissions.

The temperature was 98.6°F., the pulse 80, and the respirations 22.

The hemoglobin was 9.8 gm., and the white-cell count 16,900 with 65 per cent polymorphonuclears. In the smear the red cells were fairly normal, but the platelets were slightly increased. The urine was acid in reaction, had a specific gravity of 1.012 and gave a $+$ test for albumin; the sediment contained 2 hyaline casts, occasional finely granular casts, 15 red cells, 15 white cells and 2 epithelial

cells per high-power field. A phenolsulfonephthalein test showed 23, 20, 20 and 10 per cent excretion of the dye in a quarter, a half, one and two hours respectively. The nonprotein nitrogen was 18 mg. per 100 cc., the protein 5.9 gm., and the sulfadiazine level 5.9 mg.

A 7-gm. course of sulfadiazine was administered in the five days after admission.

An operation was performed on the eighth day after admission.

DIFFERENTIAL DIAGNOSIS

DR. JOHN W. CASS: This history could be compatible with a number of things; it raises the question of tuberculosis, abscess and some type of bronchial obstruction with slowly increasing infection. The suggestion of swollen joints and the edema cannot be evaluated as yet with the mere facts of the history. They do suggest pulmonary osteoarthropathy with some evidence of cardiac or renal failure. There is definite evidence of pulmonary disease in the x-ray films of the chest, and little evidence of congestive failure.

I do not know why "wheat-germ oil" was given. I certainly should like to know if anyone cares to offer the information.

DR. JOSEPH C. AUB: We have tried it out in cancer with equivocal results; it contains a large quantity of vitamin E. I had nothing to do with its use, however, in this case.

DR. CASS: The pulmonary process became contaminated with mouth organisms, and undoubtedly there was abscess formation, which raises the question whether it was abscess from the beginning. I should doubt this from the sequence of events; I think that the primary disease process simply became contaminated with these organisms and that abscess formation occurred.

Extreme loss of weight is compatible with lung abscess or other suppurative lung conditions, as well as tumor, malignant or benign, with or without infection.

Apparently the patient was having real pain, which is against tuberculosis and more compatible with abscess or tumor. Was more than one sputum specimen examined for tubercle bacilli?

DR. TRACY B. MALLORY: At least three sputum examinations were negative for tubercle bacilli.

DR. CASS: I think we can feel fairly confident that we are not dealing with tuberculosis. Although clubbing can occur very quickly under certain conditions, its sudden development is rare; it points against tuberculosis but is perfectly compatible with tumor plus infection or suppurative infection alone.

The physical signs I interpret as those of solid mass, with peripheral atelectasis and pleural in-

involvement as the explanations why he was having so much pain.

I should say that the edema was not associated with the heart but with kidney involvement secondary to the septic process in the chest. The urine showed evidence of kidney irritation. The serum protein was a trifle low, the albumin definitely low; the ratio was inverted so that although the total protein was not greatly below normal I think it is still compatible with sufficient kidney damage to cause some degree of edema.

May we see the x-ray films?

DR. LAURENCE ROBBINS: The entire process is on the left. This is the large cavity that is spoken of; the other areas of density in the large cavity are seen better in the lateral view and lie anterior to the large cavity. The right lung field is clear.

DR. CASS: The x-ray findings strengthen our belief that we are not dealing with tuberculosis or pure infection of any type. There is a distinct description of a mass, and it is well known that any type of malignant mass in the chest can have cavities within it or behind the obstruction that the mass causes. From the bronchoscopist's report we get confirmation of bronchial obstruction with suppurative disease in back of the obstruction. The only infectious state that would produce this would be tuberculosis with involvement of the bronchial wall as well as the parenchyma. But we have several negative biopsies, which are quite important in ruling out tuberculosis but not tumor. As a matter of fact the appearance of bronchial tuberculosis is so characteristic that the bronchoscopist would scarcely need to take a biopsy. We have not ruled out malignant tumor, however, on the basis of the negative bronchoscopic examination and biopsies.

It was apparently obvious that the suppurative situation could not be adequately drained by postural or bronchoscopic drainage, and external drainage had to be instituted.

This apparently changed the course very little, and it was necessary to readmit the patient after a month, primarily for study of his edema. His heart seemed essentially normal, and I believe his dyspnea was chiefly mechanical, perhaps due to displacement of the mediastinum. He then had a bronchial fistula, as would be expected, and no essential change in the primary disease. I still believe that the edema was secondary to the pulmonary disease. I do not attach any particular significance to the abdominal veins, in spite of the fact that they might indicate liver damage. The non-protein nitrogen was within normal limits—a bit low. The total protein was low, and the albumin-globulin ratio essentially normal. Even though

this is true, the lowered total protein was getting to the point where one would expect edema. So far as the Congo-red test goes, this rules out amyloid disease. It is rather strange how seldom one makes a clinical diagnosis of amyloid disease in suppurative diseases of the chest, but I am not sure how much significance can be placed on a perfectly normal Congo-red test.

At the third admission the patient apparently had improved a bit, unless the gain in weight was due to edema. But I believe it was probably a true gain in weight. The persistent pain I think is adequately explained as pulmonary osteoarthropathy, and he still had edema. It is apparent that the drainage was not adequately taking care of the pulmonary situation. He had reached the point where as much as possible had been gained by the drainage, and an attempt was made to correct the primary situation.

He was admitted for the fourth time for operation, pneumonectomy. It is definite that there were bronchial obstruction and pulmonary suppuration with multiple cavities, and the question is whether we can explain this process on the basis of infection alone, of tumor or of some other form of bronchial obstruction plus suppurative disease behind the obstruction. It is possible, I suppose, to have a lung abscess beginning with such a type of history as this with a gradual development of foul sputum. I cannot visualize, however, a bronchial obstruction occurring secondary to abscess, and we know from bronchoscopy that obstruction was present. The only infection that would fit the picture is tuberculosis, but we have definitely ruled out tuberculosis by the multiple sputum examinations and by the biopsy. If this man had been fortunate enough to have had tuberculosis this series of procedures would have been proper,—namely, the drainage of a large cavity and, later, a pneumonectomy,—but I believe he was not so fortunate as to have this disease. So we are left with tumor with abscess formation behind the obstruction. The tumor could be benign, but we do not have the proper history for a benign tumor. There was not the long story of cough and intermittent episodes of infection so commonly associated with this type of obstruction. A tumor was not seen on bronchoscopic examination, and although it is more or less guesswork from this point on, I should say that we are dealing with a malignant type of obstruction, in spite of the negative biopsies. The course was certainly relatively benign for the usual bronchiogenic carcinoma. We have a right to mention primary sarcoma—a very rare tumor and one that may very well fail to yield a positive biopsy. However, I think we should pick the commoner type of disease, which

is bronchiogenic carcinoma, in spite of the history of repeatedly negative biopsies.

DR. WILLIAM B. BREED: I cannot refrain from suggesting lymphoma as a strong possibility for no good reason except bitter experience in the past.

DR. JOHN W. STRIEDER: As Dr. Cass said, certainly the sequence of steps was correct and one has the right to suspect underlying disease—I certainly agree with Dr. Cass that carcinoma is the best bet.

CLINICAL DIAGNOSES

Carcinoma of lung, with necrosis and abscess formation.

Sulfonamide nephrosis.

DR. CASS'S DIAGNOSES

Carcinoma of the lung (bronchiogenic).

Bronchial obstruction, with pulmonary suppuration.

Nephrosis (septic).

Pulmonary osteoarthropathy.

ANATOMICAL DIAGNOSES

Epidermoid carcinoma of lung.

Abscess of lung.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Two interesting features invite discussion—the primary pulmonary process and the edema and the signs in the urine. Since we did not get permission for an autopsy, I cannot say anything about the kidneys, and I suppose it is profitless to speculate about them. In regard to

the lungs, total pneumonectomy was done with a preoperative diagnosis of chronic lung abscess, but with the consideration that there might possibly be carcinoma behind it. Inasmuch as they were not able to prove the presence of carcinoma, it was believed that the patient should be given the benefit of the doubt and the chance of cure by pneumonectomy.

At the time of operation it became evident as the operation progressed that the surgeon was forced to cut through neoplastic tissue close to the hilus of the lung. He had to continue at that stage with the pneumonectomy, which was successfully carried out. The operative wound healed well, with complete apparent relief of the pulmonary symptoms, but the patient slowly developed further evidence of renal insufficiency and died three weeks after operation.

The lung showed a large abscess cavity near the base of the upper lobe. The walls of this cavity consisted primarily of fibrous tissue and showed no neoplasm. Above this major abscess cavity, however, was a spherical tumor mass, in the midst of which was a second abscess cavity, and the walls of this upper cavity were neoplastic. The major abscess that was seen in the x-ray plates was, I believe, the lower benign one. That is what was drained at the first operation, and no tumor was encountered at that time. Nor was any found there when we finally had the entire lung in our possession. The bronchus leading to this area was occluded by external pressure from extension to the hilus of the tumor, which originated near the apex of the lung. The tumor was a poorly differentiated epidermoid carcinoma.

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HOSPITALS AND COMPULSORY HOSPITAL INSURANCE

"Every governmental energy must be concentrated on winning the war. Reforms or making America over cannot but dislocate the war effort." This statement by Ex-President Hoover in his twelve points of vital interest to the Home Front is so axiomatic that it should delay additional social-security legislation until the war has been won. Regardless of its virtues or defects, legislation that will profoundly affect the postwar American way of life should be postponed for consideration with other peacetime readjustments. However, since bills of this type have already been submitted to Congress and since silence might be taken for assent or approval, discussion appears to be necessary.

Such a bill, "To amend and extend the provisions of the Social Security Act; to establish a federal social-insurance system; to extend the coverage of federal old-age and survivors' insurance; to provide insurance benefits for workers permanently and totally disabled; to establish a federal system of unemployment compensation and temporary disability benefits and a federal system of unemployment offices; to establish a federal system of hospitalization benefits; to amend the Internal Revenue Code; and for other purposes," has been introduced by Representative Thomas H. Eliot, of Massachusetts. Without consideration or comment on the other parts of the bill, the proposal "to establish a federal system of hospitalization benefits," or, in other words, "compulsory hospital insurance," as it is commonly called, deserves critical comment.

At the present time in the United States there is a widespread and rapidly growing system of voluntary hospital insurance known as the Blue Cross Plan. The basic philosophy underlying such voluntary hospital insurance is radically different from that of compulsory hospital insurance, in spite of their aiming at the same objective.

Voluntary insurance, as its name implies, connotes a voluntary act on the part of the insured, as the result of consideration and decision. It requires thinking. Thus it exemplifies the essence of democracy. By thinking, choice and action the subscriber becomes a better citizen, and by the development of his will and initiative the community is benefited and improved. It is a slow process, but sure.

Compulsory insurance, likewise, is self-descriptive for it means that all persons falling within its provisions shall, willy-nilly, comply with its regulations. There is no opportunity for choice or decision. Essentially it is taxation under another name. It is regimentation held to be justifiable by the claim that it is for the benefit of the insured, that it spreads the burden and that it forces the improvident to provide. Its proponents claim that it will achieve in one year what voluntary insurance would require many years to accomplish.

and that it would eliminate charity and so increase the self-respect of former recipients. They compare by analogy the anticipated benefits of compulsory hospital insurance to the good accomplished by the Workmen's Compensation acts, forgetting that in the latter case no voluntary plan was available.

Voluntary hospital insurance has been available for ten years. New and not understood, growth during the early years was slow. It has rapidly expanded during the last five years, and now over ten million people are insured under this plan. It is spreading rapidly. Reciprocity between plans is accepted in principle and practice. In collaboration with state and local medical societies, plans for the coverage of medical fees for hospital care are being developed, and in some states are already in operation. Since it operates within state boundaries, it is adaptable to local conditions. Since it is a nonprofit corporation, it is flexible and can adjust to new conditions without resort to legislation. Since it is subject to regulation by state commissions of insurance and welfare, its subscribers are protected from exploitation. Its cost of operation has been uniformly low.

There is no opposition on the part of the American Hospital Association or of most hospital administrators to the provision of better hospitals in rural areas, to the extension of hospital care for certain public-assistance categories, such as the aged, and even to the consideration of compulsory hospital insurance. But they believe that the resulting plan should be the product of collaboration and co-operation by the Social Security Board, hospital representatives, physicians and representatives of the charitable, labor and welfare organizations of the community and that this collaboration should take place at a time when adequate and contemplative consideration can be given to a problem so vitally affecting American life. The American Hospital Association is actively furthering the extension and liberalization of Blue Cross plans, an endeavor that can go on during the emergency without hampering the war effort, since

the methods and machinery are already in operation.

Specific defects in the Eliot bill can be noted as follows:

The proposed federalization scraps the present relation provided by the Social Security Act between the states and the federal government.

The United States is too large and too varied to be adequately legislated for on a matter so vitally influenced by local conditions. States can give better adjustment and control, according to local needs.

The bill requires the setting up of a new bureau for administration and operation at a time when the manpower of the Nation is already overextended, and with the certainty of added cost.

Nothing in the bill remedies the lack of medical care and hospital facilities in rural areas. In fact, the bill expressly prohibits the use of money for this purpose.

The bill does not adequately separate administration and payments for hospitalization and disability benefits. The experiences of European plans point to the necessity of this separation.

The bill as drawn gives no consideration to the necessity of preserving voluntary plans. The present hospital system is based on the co-operation of voluntary and governmental hospitals, which supplement each other in caring for all classes of the community. If compulsory insurance is instituted, certainly a similar co-operation should be provided for with voluntary insurance. Otherwise it will probably mean the gradual destruction of philanthropy, for local interest will be difficult to sustain if the federal government assumes leadership and responsibility. Local morale suffers under remote control, and there would be no incentive for experimentation in different localities to meet varying conditions.

There is no consideration of medical-care fees, a program that is now going forward under the leadership of the voluntary plans.

The problem boils down, finally, to an evaluation of the moral values inherent in voluntary plans contrasted with the expected material values of compulsory plans. It is essentially individualism versus regimentation. Further consideration of such social readjustments should not be undertaken during the stress of war conditions, but should be put off for consideration after the war is won. Probably a satisfactory compromise between the two extremes can then be obtained.

DIPHTHERIA CARRIERS

THE care of the diphtheria carrier has been a perplexing problem for the last fifty years. So many different measures have been heralded as effective and have later . . . to be valueless that one is wary of any

ward. It has long been known that the hazard of the tonsillar carrier is usually eliminated by tonsillectomy. Furthermore, the removal of a small ball of cellophane or a piece of rubber sponge from a child's nose has promptly brought about a series of negative release cultures. However, when tonsils have been removed and the question of a foreign body in the nose has been eliminated, the experienced physician has learned that other measures aimed at the destruction of the diphtheria organism not only have proved to be futile but have made matters worse by injuring the mucous membrane.

A valuable contribution to the carrier problem has been made by Boissard and Fry* in England. From an elaborate and painstaking study of 388 cases of diphtheria, these authors have found that the presence of substantial numbers of hemolytic streptococci in the nose was frequently responsible for the persistence of positive diphtheria cultures and that, by elimination of the streptococcal element with local applications of sulfanilamide, the diphtherial element promptly disappeared. No drug of the sulfanilamide group has been shown to have a direct influence on *Corynebacterium diphtheriae*, either in vivo or in vitro; therefore, these drugs have no effect on the course of diphtheria. The administration of antitoxin still remains the first principle in the treatment of the disease, but it is of no value in the treatment of the healthy carrier. Indeed, the value of antitoxin in treatment of the disease does not depend on any direct action on the diphtheria organism but on the neutralization of the circulating toxin; this permits the natural protective forces of the body to attack the localized infection effectively. The internal administration of sulfanilamide, as well as its local application, has been tried on carriers, but with unsatisfactory results. These English authors, however, have proved that the drug is effective in nasal carriers in whom *C. diphtheriae* is associated with substantial numbers of hemolytic streptococci.

The treatment consists in insufflating sulfanila-

mid powder into the nose twice a day for a week. During the following week, cultures are taken every other day. If all these are negative, the patient is released; otherwise, the process is resumed for another week. These authors obtained abrupt and permanent elimination of the diphtheria-carrier state in 24 of 26 nasal carriers after the first week's treatment. In 8 cases of tonsillar carriers, the insufflation of sulfanilamide in the nose and its direct application to the tonsils proved ineffective.

The scholarly attitude exhibited in the report of this experiment offers convincing evidence that a significant step, with well-defined limitations, has been made in the elimination of the diphtheria carrier.

MEDICAL EPONYM

SIPPY TREATMENT

The first account by Dr. Bertram W. Sippy (1866-1924), professor of medicine in the Rush Medical College, of his method of treating peptic ulcer appeared in the third volume (pages 342-353) of *A Handbook of Practical Treatment* (Philadelphia and London, 1917), edited by John H. Musser and A. O. J. Kelly. He writes:

... Undoubtedly, hyperchlorhydria is unfavorable to the healing of ulcer. . . . The indication in medicinal treatment should be to reduce the corrosive action of the gastric juice, to diminish the mechanical irritation caused by food, pressure, peristalsis, and active movements of the body, to provide adequate nourishment and to treat the symptoms and complicating conditions as they arise. . . . During the first five days no food or drink is given by mouth. . . . At the end of five or six days one may begin to feed half an ounce each of milk and cream every hour from early morning until eight or nine o'clock at night. . . . Midway between each feeding a powder consisting of 10 grains each of calcined magnesia and sodium bicarbonate may be given alternately with a powder of 10 grains each of bismuth subnitrate and sodium bicarbonate. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SOCIETY HEADQUARTERS

Owing to the shortage of fuel oil, the Boston Medical Library will be closed on Saturdays, commencing December 19 and continuing until further notice. This will

*Boissard, J. M., and Fry, R. M. Chronic nasal diphtheria carriers cured with sulfanilamide. *Lancet* 19610 614, 1942.

necessitate the closing of the headquarters of the Society and the office of the *Journal* during the corresponding period. In an emergency, the officers of the Society and the managing editor and associate editors of the *Journal* can be located through their offices or homes.

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

TOXEMIA AND ECLAMPSIA

Twenty-seven maternal deaths during 1941 were attributed to toxemia and eclampsia. The term "eclampsia" in this classification applies to pregnant patients who had actual convulsions. Among these patients, there were 7 with convulsions and 1 with a severe toxemia but no convulsions who were delivered by cesarean section. This is noteworthy, since it is generally accepted that undelivered eclamptic patients who are not in labor have the best chance of recovery if they are treated with extreme conservatism. Twenty-five years ago, convulsive patients not in labor were treated by *accouchement forcé*. Because of the extremely high mortality of the patients so treated, manual dilatation of the cervix and subsequent operative delivery gradually came to be frowned on, so that today it is gratifying to note that not one case of eclampsia in this series was so treated. After *accouchement forcé* had been discarded, the belief that emptying the uterus removed the cause of disease and thus enhanced the patient's chance of recovery led to a very general adoption of cesarean section as the treatment of this complication. That any operative interference was ill advised was first brought out by the Stroganoff method of treating eclampsia. Some modification of this conservative method has been proved to be the accepted method of procedure. In some clinics, nothing is done other than sedation of the patient and the intravenous administration of magnesium sulfate—there is no operative intervention. To this conservative treatment, other clinics have added artificial rupture of the membranes for the purpose of inducing labor, and statistics in the clinics where such cases are so handled are so much better than those where cesarean section is done that the latter has been practically abandoned. This being so, it is interesting to analyze the fatal cases of eclampsia delivered by cesarean section.

The first patient was a primipara who died forty hours following a classical cesarean section. The prenatal care was sketchy and probably not ade-

quate. She was about seven months pregnant when three convulsions occurred. A 2½-pound baby, who lived for a short while, was delivered. This case quite probably would not have been fatal had the convulsions been treated symptomatically by intravenous magnesium sulfate, sedatives and, possibly, induction of labor by artificial rupture of the membranes. It is fair to say that the method of treatment in this case would not have obtained in most clinics.

The second case was that of a patient seven and a half months pregnant who had been showing pre-eclamptic symptoms—a systolic blood pressure of 140 and a large trace of albumin in the urine. Because of this she was sent to the hospital for delivery by cesarean section on the following day. During the night the blood pressure rose to 180, and while she was being prepared for operation, a convulsion occurred. A living premature baby was delivered by cesarean section, but the patient did not regain consciousness. In view of the present knowledge of obstetrics, conservatism might have averted this fatality. The prenatal care in this case was adequate if not the most intelligent.

The third case was that of a primipara who had had a previous nephrectomy. She was followed intelligently during the prenatal period but when about thirty-four weeks pregnant developed marked edema and a systolic blood pressure of 180. In spite of hospitalization, the toxemia did not abate; cesarean section was done and a living child delivered. Nine days postpartum convulsions appeared, and death followed within twenty-four hours. Unfortunately there was no autopsy. The late post-partum eclampsia probably means that the remaining kidney suffered permanent damage, which resulted in total kidney failure. In all honesty, it seems unlikely that the cesarean section was much more than a contributing influence in this fatality.

The fourth patient was a primipara approximately at term whose prenatal care was neither intelligent nor adequate. Convulsions occurred before labor, and a cesarean was done because the cervix was not "favorable." Death occurred thirty-six hours after delivery.

The fifth patient had had a previous cesarean section in 1933. She was adequately taken care of prenatally, and at the seventh month was hospitalized because of a systolic blood pressure of 170. Hospital treatment did not relieve the toxemia, and when the patient was about seven and a half months pregnant an extraperitoneal cesarean section of the Waters type was done, but death occurred a few hours after delivery. This patient

may have had myocardial failure, which occurs occasionally in patients with severe toxemia. As she was not in labor and as the membranes had not been ruptured, it is difficult to understand why the Waters operation was performed. In this case, convulsions did not occur.

The sixth case was that of a primipara who, at approximately seven and a half months, developed toxemia associated with vomiting of blood, jaundice and a systolic blood pressure of 220. Hospitalization was recommended and accepted. The morning of the entry the patient's blood pressure came down to 164 systolic, 100 diastolic, but rose to 230 systolic, 120 diastolic in the afternoon. A classical cesarean was done under spinal anesthesia, and a living baby weighing 2 pounds, 12 ounces, was delivered, death occurred shortly after delivery. One can only wonder whether conservatism would have averted this catastrophe.

The seventh patient was a multipara who had had six previous pregnancies and was said to have had toxemia in her second and fourth pregnancies. In the seventh month of her last pregnancy the systolic blood pressure rose to between 160 and 200, and she was hospitalized. Convulsions occurred and increased in severity, and consequently a cesarean section was performed. Death occurred thirty-two hours later. The history of this case is not adequate and, of course, a cesarean section in a multipara with eclampsia has no justification.

The history of the eighth and final case is not adequate. Eclampsia existed in a patient on whom a cesarean section was performed, presumably an autopsy was done because the diagnosis of focal necrosis of the liver was made.

(To be concluded)

DEATHS

FRENCH—RALPH W. FRENCH, M.D., of Fall River died December 7. He was in his sixtieth year.

Born in Fall River, he attended Harvard University and received his degree cum laude from Harvard Medical School in 1910. After serving his internship at the Massachusetts General Hospital he joined the staff of the Truist Hospital.

He was a fellow of the Massachusetts Medical Society and the American Medical Association. He was also a member of the American College of Surgeons, the New England Surgical Society and the Fall River Medical Society.

His sister and an aunt survive him.

KENEALY—JOSEPH H. KENEALY, M.D., of Natick died in Chicago, December 2. He was in his sixty-fifth year. Born in Natick, he received his degree from Harvard Medical School in 1900. He practiced in Boston for several years before taking up residence in Chicago. He was a former member of the Massachusetts Medical Society.

His widow and a daughter survive him.

WAR ACTIVITIES

CIVILIAN DEFENSE

RED CROSS MOBILE CANTEENS

The following directive was recently forwarded to all regional directors, regional medical heads and deputy regional medical heads of the Massachusetts Committee on Public Safety:

* * *

1. Some misunderstandings may have developed due to the fact that medical mobile canteens were not mentioned in *Medical Handbook No. 2* of the Massachusetts Committee on Public Safety. The Red Cross has agreed to provide a determined number of such mobile canteens properly equipped and with trained personnel that shall become the local units of the Medical Division in supplying civilian war aid, although maintaining their identity and insignia. Should the situation be of such magnitude to require additional assistance, the Medical Division will then call, through appropriate channels, on the Massachusetts Women's Defense Corps, held in reserve for such purposes, or on whatever other supplementary resources are available. Local plans at variance with these terms shall on request of any party, be submitted to the executive director of the Massachusetts Committee on Public Safety for amendment or approval by him after consultation with the Red Cross.

2. The determined number of mobile canteens varies not merely with the population but with local needs. In some communities one mobile canteen may be sufficient to service two or three towns combining two or three medical first-aid posts, in others the ratio may run as high as one mobile canteen for each medical first aid post. In the larger cities where several first aid posts are included in one medical depot, a ratio of 40 per cent of the number of auxiliary ambulances involved is the accepted quota.

3. Auxiliary ambulances accompanying the physicians and their medical units should be the first to arrive at the scene of the incident, but mobile canteens with hot liquids for the treatment of shock should not be far behind.

4. Heretofore, in most localities, mobile canteens have not participated in practice alerts. With the adoption of the audible signal for yellow or green lights, it will now be necessary for these units to mobilize.

It is suggested that plans be developed between chief medical officers and Red Cross liaisons whereby mobile canteens shall proceed to the prearranged spot where they plan to obtain their supply of hot liquids and so forth, and stand by for instructions from the chief medical officer whether to prepare and load such hot liquids, to proceed to the medical depot, medical first aid post or incident or to dismiss. Where canteen equipment is stored at the medical depot this procedure will be unnecessary in practice alerts, but in any case mobile-canteen vehicles must mobilize on the preliminary audible signal. Chief medical officers must remember they are standing by and not forget to dismiss them.

A. WILLIAM R. REGIO, Surgeon (R), USPHS
Director, Medical Division

JOSEPH R. HAMILLEN, American Red Cross Liaison
First Service Command

19 Tremont Street
Boston

MISCELLANY

TUBERCULOSIS IN COLLEGE STUDENTS

A second five-year review of tuberculosis in college students, marking the close of a decade of service by the Tuberculosis Committee of the American Student Health Association, reveals heartening progress, along with the stern challenge that tuberculosis still clings tenaciously to first place among causes of death in those of college age. Three hundred and four colleges and universities reported tuberculosis programs for 1940-41 as against one hundred and four in 1936-37, but this represents a bare 36 per cent of American institutions of higher education. Ancient and erroneous notions about tuberculosis still persist in the minds of many college administrators, which unhappily limit the adequacy of their college health services. The truth must be carried to these people ceaselessly and convincingly, if tuberculosis is to be dislodged from the American college campus. The following abstract of a recent article on the subject (Lyght, C. E. Tuberculosis in college students: a second five-year review. *Am. Rev. Tuberc.* 46:227-237, 1942) is of interest.

The Tuberculosis Committee of the American Student Health Association was formed in 1931 following the first National Conference on College Hygiene at Syracuse University. At that time six institutions of higher education were known to have begun tuberculosis programs—the state universities of Minnesota, Michigan and Pennsylvania, Western Reserve University, Vassar and Yale. At the close of the first five years of the Committee's work, fifty colleges reported programs. Now, at the end of the second five years, three hundred and four institutions so report. This number represents every section of the country, and includes endowed colleges and universities, state colleges, institutes, teachers' colleges and universities, and civic colleges and universities. State universities made the best showing; the small, privately endowed colleges the least satisfactory.

In 1936-37 there were ninety-one colleges using the tuberculin test on 56,224 students; in 1940-41, two hundred and fifty-five colleges were doing so, and the number of students taking the test had increased to 149,744. The percentage of institutions using the Mantoux method dropped in this period from 88 to 82. Recent experiments in some localities with patch testing, along with some schools using the Pirquet method because the state supplies only that type of testing material, account for the drop.

The number of colleges using routine chest films without prior tuberculin testing increased from 12 per cent in 1936-37 to 16 per cent in 1940-41. A few colleges and universities have adopted miniature-film mass surveys.

There has been an encouraging increase in the number of colleges examining nonstudent personnel. In 1936-37, thirty colleges required the examination of food handlers, and twenty-nine the examination of the faculty and administrative employees, while in 1940-41 there were one hundred and eight colleges reporting the examination of food handlers and ninety-two the examination of the faculty and administrative personnel.

The annual reports of the Tuberculosis Committee have disclosed a startling difference in the amount of tuberculosis in students discovered in colleges with case-finding facilities and in schools with no program of case finding. In the second five-year period, 1936-41, the colleges in the latter category reported the discovery of 184 new cases of tuberculosis among a student enrollment of

668,895, a rate of 27.5 per 100,000. The colleges with case-finding facilities reported the discovery of 3523 new cases in a student enrollment of 1,850,755, a rate of 190.5 per 100,000, during the same period.

Roughly, this confers a ratio of 7:1 in favor of the progressive colleges dedicated to the proposition that tuberculosis must be tracked down to its lair, found early and treated promptly, if it is to be defeated ultimately in the individual and in the Nation. These figures imply that thousands of cases of tuberculosis, many of them infectious, are being harbored and ignored among American college students through utter failure of most colleges to comprehend that a threat to health truly exists and that a major social and economic problem clamors for action.

Letters from college administrators attempting to justify the nonexistence of case-finding programs in their respective institutions indicate the prevalence of such ancient ideas as, that only when "consumption" arrives is tuberculosis present, that early tuberculosis can be ruled out by a physician's cursory certification or by stethoscopic search, or by stratified social selection. The survival of these fallacies among educated people represents our failure to carry the truth ceaselessly and convincingly to every person whose information, no matter how complete in most directions, remains barren with respect to tuberculosis.

The war, which in its train brings conditions of overcrowding and overwork, the disruption of public and private medical services, the curtailment of budgets and the restriction of personnel, gives opportunity also for the increase of tuberculosis unless special efforts are made to guard against this menace. Army, Navy, industry, public health—all must fight together and against tuberculosis, but it is of the very essence and function of education that colleges and universities lead the battle.

It is suggested that just as counties were once accredited for eliminating tuberculosis from their dairy herds, even as today they are being accredited in Minnesota for driving death rates and infection rates to low levels, colleges and universities might be accredited by the American Student Health and the National Tuberculosis associations, once they have inaugurated and maintained acceptably a modern program against student tuberculosis. Laggard colleges might thus be tempted to make the necessary adjustments so that they could be listed on the Roll of Honor of progressive, public-spirited institutions.

The war must go on. The war must be won, and we must win it, both from our external foes and from such borers-from-within as tuberculosis. —Reprinted from *Tuberculosis Abstracts* (December, 1942).

BOOK REVIEW

War Department. Technical Manual TM 8-240. Roentgenographic technicians. 8°, paper, 223 pp., with 109 illustrations. Washington, D. C.: Government Printing Office, 1941. 35 cents.

This manual contains about 70 pages of descriptive material and a series of reproductions to show the position of the patient and the resulting radiograph. The descriptive material includes several chapters on the physics of magnetism and electricity, as well as chapters on the operation of an x-ray machine. The material as presented is in general correct, although there are a number of minor errors that might easily have been corrected had the manuscript been submitted to a physicist before printing.

(Notices on page x)

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TREATMENT OF ARTHRITIC CONTRACTURES OF THE KNEE

JOHN G. KUHN, M.D.*

BOSTON

DEFORMITIES at the knee are among the commonest and most disabling conditions in chronic arthritis, occurring next in frequency to deformities of the hands and feet. Five hundred and eighty-six contractures at the knee (in 313 patients) were found in 1453 patients suffering from chronic arthritis on the wards of the Robert B. Brigham Hospital. A contracture is defined as a relatively fixed shortening of a group of muscles and their ligaments. This shortening develops rapidly within a few weeks. After it has been present for several years, it often leads to irreversible changes in the muscles. The relative frequency of the various types of contractures is given in Table 1. Most of these deformities were

of the tibia on the femur and external rotation of the tibia on the femur. Subluxation of the tibia



FIGURE 1 Flexion Contracture of 20° (the usual type of deformity)

TABLE 1. Classification of Types of Deformity in 313 Arthritic Patients

DEFORMITY	NO OF CASES	PER CENT
Flexion (more than 10°)		
Simple	504	80.5
With ankylosis of tibia and femur	32	5.1
With subluxation of tibia	19	3.6
With external rotation of tibia	7	1.1
Extension (10° or less of flexion)		
Simple	17	2.8
With ankylosis of tibia and femur	7	1.1
With knees showing no contracture	40	6.4
Total	626	

simple flexion contractures, since this is the usual position that the knee assumes when an inflammation is present¹ (Fig. 1). Flexion contractures of less than 10° were not included in this study because, so far as could be observed, little disturbance in function resulted from such a mild deformity at the knee joint.

Eighty per cent of the cases were uncomplicated flexion contractures. Secondary deformities complicating the flexion contractures were found much less frequently. These, in the order of frequency, were ankylosis of the tibia and femur, subluxation

occurred only with partial disintegration of the joint surfaces² and with the absence of protection at the back of the knee joint (Fig. 2). External

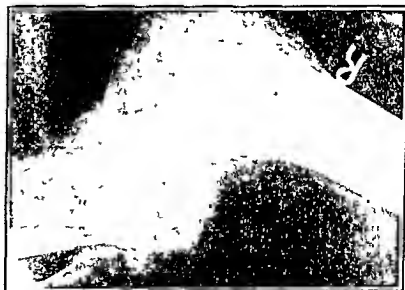


FIGURE 2 X-ray Photograph Showing Subluxation of the Tibia on the Femur.

rotation was usually associated with valgus of the foot and with prolonged muscular spasm in the biceps femoris muscle. Ankylosis of the femur

*Chief of Surgical and Orthopedic Staffs, Robert B. Brigham Hospital, Boston.

and tibia was often the end stage of the arthritis process.³

Extension contractures occurred in 2.8 per cent of the knees. These were recorded only if the knee could not be flexed more than 10° from the fully extended position (Fig. 3). This type of contrac-



FIGURE 3. Extension Contracture of Both Knees (about 5° of motion in the right knee, none in the left).

ture was observed only when the knee was kept in extension for long periods during the active stage of the disease,⁴ or when much force had been used in the correction of a previous flexion deformity.⁵ In 7 cases, the extension contracture was complicated by ankylosis of the tibia and femur.⁶

Involvement of the knee by atrophic arthritis caused all the contractures except 11, which occurred as the result of hypertrophic arthritis. Usually, both knees were similarly involved in the same patient. But there were 40 patients with flexion contracture in one knee and no deformity in the other. The case histories of these patients suggested that local trauma played the major part in this involvement of one knee only.

The deformities that disturbed function to the greatest extent were flexion contractures of more than 30°. Symptoms of sprain soon appeared not only at the knee but also at the hip and foot. Subluxation and external rotation usually increased the symptoms. With flexion contractures of less than 20°, function at the knee was not always disturbed, but weight bearing on these flexed knees tended to increase the deformity. Minimal contractures (less than 10° of flexion) rarely led to significant symptoms unless there was much bony proliferation about the margins of the knee joint. In the mildest contractures, the deformity usually did not change if the arthritis was quiescent.

When the range of motion was greatly restricted in both flexion and extension, or when an ankylosis was present, there was little evidence of sprain at the knee; however, it was usually found in the low back and hip, less commonly at the foot and ankle. Extension contractures rarely produced a strain at the knee, since weight was borne with

the knee almost fully straight. But walking led to ache at the hip and ankle because excessive motion was demanded at these joints. Extension deformities were particularly disabling if the patient's work required much flexion of the knee.

To prevent and to correct these contractures of the knee, a program of treatment was evolved that has been modified as more effective methods have been found. In patients seen during the first six months of the arthritis, contractures could usually

TABLE 2. Program of Treatment of Contractures.

TREATMENT	INDICATION
<i>Prevention of Contractures</i>	
Avoidance of weight bearing	Pain on walking and articular inflammation
Splinting in full extension	Muscular spasm with tendency to flexion
Exercises	Weakness of muscles
<i>Correction of Flexion Contractures</i>	
Series of plaster casts	Contractures not corrected passively
Pad behind upper end of tibia	Early subluxation
Internal rotation of lower leg in plaster cast	Internal rotation of tibia
Caliper when standing	Knee too weak to maintain extension on standing
Exercises	Weakness of muscles with no pain on motion
Manipulation	Adhesions limiting motion in one direction only with no inflammation
Posterior capsulotomy	Resistant flexion contracture with little destruction of articular surfaces
Traction (skeletal)	Flexion or subluxation after operation
Osteotomy	Knee fixed in bad position for weight bearing
Arthroplasty	Stiff joint
<i>Correction of Extension Contractures</i>	
Plaster casts in flexion	Fixation of knee in extension
Lengthening of quadriceps tendon	Resistant extension contractures

be prevented. Unfortunately, most of the patients came for treatment only after contractures had developed. The program of treatment and the usual indications are given in Table 2.

The most effective method of preventing contractures at the knee when arthritis was present was rest in full extension until the muscular spasm and pain had subsided. Walking was permitted when motion and weight bearing did not lead to pain. If the period of rest was prolonged beyond two weeks, exercises were often necessary to maintain strength and control of the muscles about the knee. Splinting of the knee in extension was required if there was a persistent tendency to flexion. Fixation was not continued longer than one week without examination of the knee and allowance of a little motion temporarily. Long fixation of the knee without motion tended to produce extensive muscular atrophy and a contracture in extension.

When a flexion contracture could not be corrected passively, an attempt was made to correct

it by a series of plaster casts (Fig. 4). With the fixation of a plaster cast, the muscular spasm usually subsided, and the knee could then be brought into more extension. After two days the plaster

effective method of correction in the resistant contractures was a posterior capsuloplasty, an operation in which the contracted posterior muscles and ligaments are lengthened.⁹ When there was much

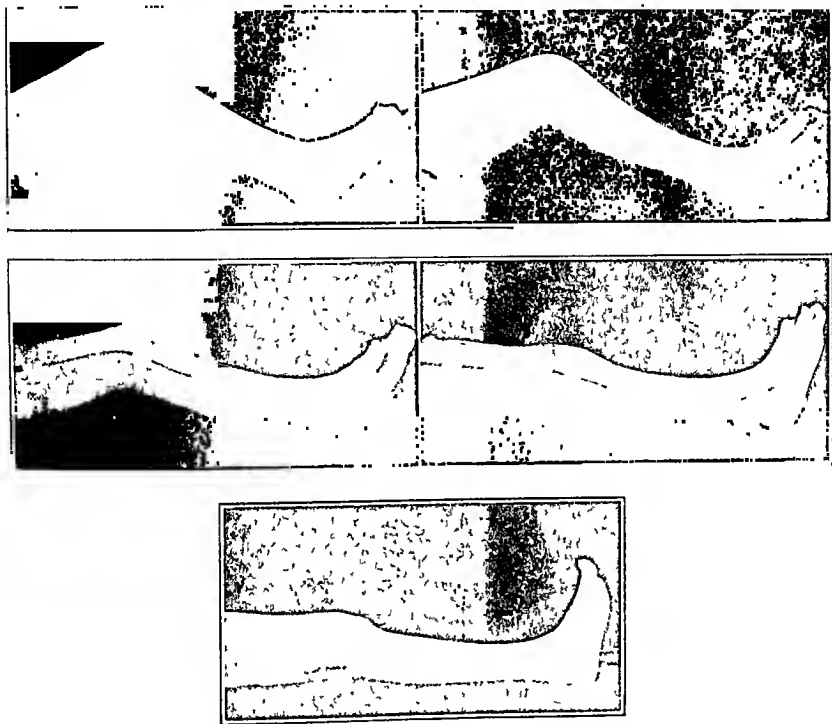


FIGURE 4 *Gradual Correction of Flexion Deformity by Plaster Casts*

cast was cut into an anterior and a posterior half and was removed for short periods to permit the application of heat and for exercises when these could be performed without pain. When 10° or more of correction in the contracture had been obtained, a new cast was applied. Contractures were usually corrected by this method in from one to three months.⁷ For persisting weakness of the muscles of the thigh, a caliper was worn when the patient was walking, to maintain correction until the muscles became stronger.

When contractures did not show correction after the use of a plaster cast for several weeks, a manipulation was considered⁸ if motion was restricted in one direction only and if there was no evidence of inflammation in the joint. Usually, the most

destruction of the articular surfaces and motion was greatly restricted, an osteotomy¹⁰ usually led to a better functional result, with less pain on weight bearing, than a posterior capsuloplasty. Skeletal traction was used only after an operative procedure such as posterior capsuloplasty, particularly for the correction of subluxation of the tibia on the femur.

When there was complete destruction of the articular surfaces, with little or no motion in the joint, an arthroplasty¹¹—an operative attempt to form a new joint—was considered if the disease was inactive. Usually, this operation was performed on one knee only, since a certain amount of stability was always lost in the attempt to secure motion. More difficulty was encountered in the cor-

rection of extension contractures than in the treatment of flexion contractures. In the absence of ankylosis, an attempt was made to secure greater motion in flexion by a series of plaster casts holding the knee in flexion. Exercises and the pull of

The poor results shown by 23 per cent were due chiefly to failure to maintain correction after the operation was performed. In recent years, full correction of the contracture after the operation has been maintained by skeletal traction or by a plas-

TABLE 3. Results of Treatment of Flexion and Extension Contractures.

TREATMENT	TOTAL NO OF CASES	GOOD RESULT		FAIR RESULT		POOR RESULT	
		NO OF CASES	PER CENT	NO OF CASES	PER CENT	NO OF CASES	PER CENT
<i>Flexion Contractures</i>							
Series of casts followed by caliper	550	97	28	80	33	173	49
Exercises alone	51	21	26	11	14	49	60
Posterior capsuloplasty	48	19	40	18	37	11	23
Manipulation	44	0	—	16	36	28	64
Arthroplasty	20	2	10	6	30	12	60
Traction (all types)	15	3	20	2	13	10	67
Synovectomy	8	2	25	0	—	6	75
Wedging (forefeet)	8	2	25	2	25	4	50
Osteotomy	3	1	33	2	67	0	—
Arthrodesis	1	0	—	1	100	0	—
<i>Extension Contractures</i>							
Casts	15	1	7	3	20	11	73
Exercises	9	2	22	2	22	5	56
Manipulation	4	0	—	1	25	3	75
Lengthening of quadriceps	1	0	—	1	100	0	—
Arthroplasty	1	0	—	1	100	0	—

gravity were also employed. When these procedures proved ineffective, a plastic lengthening of the quadriceps tendon¹² was considered.

The types of treatment used and the end results are presented in Table 3. The results of treatment are listed as good with a final result of less than 5° of contracture; fair with from 5 to 15° of contracture remaining; and poor when there was more than 15° of persisting contracture. In flexion contractures, a series of plaster casts was most frequently used. Much better results would have been shown if the contractures had been selected primarily for this treatment. Plaster casts were used in the early treatment of almost all patients. Of the 173 contractures not corrected by plaster casts, 42 were of more than ten years' duration, and 55 had been present over five years. Most of the contractures of long duration and of severe degree required surgical correction later. There is no satisfactory method of determining the resistance of contractures at the first examination. One can usually tell whether plaster casts will be effective only after several weeks of trial. Exercises alone, which were used only for the mildest flexion contractures or as palliative measures, relieved the deformity only when it was of short duration and slight degree. In most cases, exercise failed to prevent an increase in the deformity. It is not considered an effective form of therapy for arthritic contractures, and should be used only in combination with some form of support to the knee.

Posterior capsuloplasty resulted in full correction of the flexion deformity in 40 per cent of the cases.

ter cast. Skeletal traction after the manner of Russell¹³ was particularly helpful in the correction of severe subluxations of the tibia.

When the patella was bound to the femur by adhesions or by ankylosis, it was necessary to free it to permit full contraction of the rectus femoris muscle (Fig. 5). In three posterior capsuloplasties,



FIGURE 5. Ankylosis of Patella to Femur

the patella was removed, and in three others it was loosened from the femur and then covered with fascia lata. About equally good results were obtained with these methods. No correction of a flexion deformity was maintained when the patella remained fixed to the femur.

The results of manipulation were disappointing. No deformity was fully corrected, and only 36 per

cent were improved. In 4 cases ankylosis in extension occurred after manipulation and in 4 others fracture of the femur occurred during manipulation. Manipulation should be reserved for the correction of contractures of short duration, with limitation of motion in one direction only, in the presence of inactive disease and with no great atrophy of bone or muscle. The only advantage of manipulation is that in selected cases it may release adhesions that cannot be corrected by plaster casts alone.

Arthroplasty for the relief of bony ankylosis at the knee was performed in 20 cases. The poorest results were observed when a great amount of flexion was present before arthroplasty. In such cases, skeletal traction or a series of plaster casts was used to correct the flexion after operation. Arthroplasty was far less effective in chronic arthritis than in ankylosis after trauma or acute infections.

Traction was not an effective method of correcting flexion contractures. Improvement was obtained in only a third of the cases in which it was used. Even skeletal traction was too painful in contractures of long duration to be effective, beneficial results were obtained only after operative procedures in which the contracted muscles and ligaments had been released.

Synovectomy¹⁴ was not used to correct a contracture primarily. At times, it aided the correction of deformity by permitting increased motion at the knee. This operation, planned for the removal of inflamed and thickened tissue from the knee joint, sometimes led to an increased range of motion when motion was hindered by the thickened tissue.

Wedging casts and forceful stretching of the knee with special apparatus were not effective in arthritic contractures. Although correction sometimes resulted in the less resistant contractures, greater stiffness of the knee joint usually followed. In the resistant contractures, pressure sores often developed before much if any correction was obtained.

Osteotomy, a procedure rarely used, led to an improved position for function. This method resulted in no increased motion but gave a better position for weight bearing. Osteotomy, rather than posterior capsuloplasty, was employed when there was little motion in the joint and extensive destruction of the articular surfaces. Usually, in arthroplasty was the operation of choice.

Arthrodesis,¹⁵ although it prevented deformity by eliminating motion at the knee, was not a popular procedure. Only one such operation was performed. Four other patients who had an arthrodesis performed on the knee joint before coming

to the hospital stated that they preferred a painful, movable knee to a stiff, painless one. It is a justifiable treatment in chronic arthritis only when there is marked destruction of the joint, with persistent pain on weight bearing, in a patient who must stand at his work.

The treatment of extension contractures has not been encouraging. The results were considered good if the knee could be flexed 60° from full extension, fair if the knee could be flexed 45° to 60° and poor if there was less than 45° flexion. With less than 45°, the patient was unable to climb stairs normally, or to use the leg in rising from a seat. Casts rarely led to an improvement of an extension contracture. Gravity and exercises would be expected to lead to increased flexion, but these were also relatively ineffective. A plastic lengthening of the quadriceps tendon seemed to be the most effective treatment for extension contractures of long duration.

CONCLUSIONS

Arthritic contractures at the knee can be prevented by rest, if weight bearing causes pain, by splinting of the knee in full extension, if there is muscular spasm, and by exercise, if there is muscular weakness and atrophy.

When flexion contractures cannot be corrected passively, the best early method of correction is a series of plaster casts, each cast securing as much extension as possible. Calipers and exercises are usually required to maintain full correction until muscular strength is regained.

Flexion contractures too resistant for plaster casts are corrected most easily by a posterior capsuloplasty, which leads to painless weight bearing if the articular surfaces are not destroyed. Manipulation, wedging casts and traction are relatively ineffective procedures. Skeletal traction is of value only after operations that free the contracture and permit extension gradually or after the correction of a subluxation.

Arthroplasty is the procedure of choice in ankylosis if motion is desired, but not in chronic arthritis. Osteotomy is employed when a better position for weight bearing alone is desired.

Plastic lengthening of the quadriceps tendon seems to be the most effective treatment for extension deformities, in general, the treatment of such contractures is not encouraging.

377 Marlborough Street

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IMPORTANT CLUES IN CARDIOVASCULAR DIAGNOSIS*

PAUL D. WHITE, M.D.†

BOSTON

IT IS of great value in the practice of medicine to keep clearly in mind certain simple diagnostic rules and diligently to seek various important clues to diagnosis. This is particularly true in the study of patients with cardiovascular symptoms or signs. A complete and accurate cardiovascular diagnosis can often be made by the realization of the significance of a single symptom or sign or by a single well-placed question. It is of special interest also that the very multiplicity of symptoms in a nervous person is encouraging evidence of a large nervous as contrasted to an organic cardiac responsibility for illness. The more symptoms, often the less disease.

SYMPTOMS

Pain. Substernal tightness, not often dignified as pain at first, beginning on effort after breakfast on a cold morning in the fall, usually mild the first week or two, and occurring in a business or professional man in the fifties, is, in my experience, the commonest type of onset of angina pectoris due to coronary heart disease. Usually, angina pectoris is a pressure sensation, which is often described by the patient as a difficulty in breathing, and sometimes, therefore, gives rise to an erroneous diagnosis of dyspnea from some cause or other. The patient may say that it is not pain to him, but neither is it true breathlessness. Thus it is important to analyze this symptom in detail. The physician should not use the word "pain" alone in his questioning.

Angina pectoris is often mild, especially at its onset. It does not need to be severe; it may be merely a sensation of slight pressure on some effort that would not normally bring it on. The amount of exercise is more important than the amount of pain. The presence of even mild substernal discomfort on effort is more important than the severity of the pain. The severity of the discomfort or pain is largely dependent on the sensi-

tivity of the person. A sensitive, nervous person will feel the pain more acutely. If slow walking alone brings on mild oppression, this is much more significant than if the pain, no matter how severe, is produced by a faster gait.

Angina pectoris almost invariably occurs at first on effort. If it comes at rest (angina decubitus) one is dealing with an acute coronary occlusion, with or without myocardial infarction. Or else there is some other cause for the pain, perhaps a gastric condition (cardiospasm) or some responsible lesion in the chest other than heart disease.

Meals predispose to angina pectoris on effort, especially breakfast. The patient tends, during the day, to get his second wind, as one might say, and is able to do things after supper or lunch more readily than after breakfast.

Often a patient does not speak of this symptom for days or weeks after it first appears; maybe he does not mention it for years. I have found that especially characteristic of physicians.

The pain tends to be a waxing pain. When the person affected walks a little faster or uphill, the pain grows more and more severe. As a rule, it is a continuous pain until the person stops—continuous, but lasting only a few minutes. It is not a throbbing pain; it is not a sharp pain; it is not a stab; it is not a prolonged ache.

The commonest age at which angina pectoris first appears is the fifties; fifty-two or fifty-three is the average of such patients whom I have seen in the last twenty years. They range, however, from the thirties up to the eighties, but most of them are still active in their work long before retirement. Business or professional men are especially affected; business and professional women may have such symptoms too, but much less commonly. Housewives appear to have angina pectoris less frequently than do business and professional women.

The one most striking etiologic relation of angina pectoris is that of sex. It is preponderantly

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†Lecturer in medicine, Harvard Medical School; physician, Massachusetts General Hospital.

a man's disease. It is essential to remember that women under fifty rarely suffer from true angina pectoris or other manifestations of coronary heart disease, which in the earlier years of life is, as just stated, largely confined to men. The few younger women who do develop it almost always have either hypertension or diabetes mellitus, or else there is a strongly suggestive family history. Those women who have a family history of angina pectoris or coronary heart disease in both branches of the family or in their maternal ancestors alone at young ages, have a tendency to angina pectoris under fifty, even without hypertension; however, this is rare. If a woman is under fifty, chest pain is probably not evidence of heart disease.

Substernal discomfort coming on when seated or recumbent but not on effort is not due to coronary insufficiency; it is most likely of gastric origin, and due to cardiospasm, quite possibly secondary to gastritis from an hiatus hernia. It is vital to distinguish angina pectoris from the heartache over the left breast which is commonly found in other conditions, especially indigestion and nervousness. Tenderness on pressure or palpation over the precordium decreases very much the clinical significance of heart pain, which usually turns out to be only the heartache of neurocirculatory asthenia or pectoral muscle strain.

Another vital point is this: in the presence of prolonged precordial pain, with or without a pericardial friction rub, a definite exacerbation of the pain on deep breathing means acute pleuropericarditis and not coronary thrombosis with myocardial infarction. Misinterpretation in such cases has probably caused frequent errors in diagnosis. Thus, one of the most valuable test questions of all concerns the effect of deep breathing. If in a patient with precordial pain a deep breath increases the pain or perhaps is the chief cause of it, a diagnosis of pleuropericarditis is indicated. The change in the electrocardiogram is atypical and often transient. Cardiologists are now beginning to separate from the large number of patients diagnosed as having coronary thrombosis certain exceptions like the foregoing, with various conditions that may simulate coronary heart disease.

An accurate history will almost invariably enable one to establish the correct cardiac diagnosis. The history is the essential part of the differential diagnosis of heart disease. As already stated pain that comes on when seated or recumbent but not on effort is most likely of gastric origin, and perhaps due to an hiatus hernia. Such pain is often actually improved by standing and walking about; the stomach settles away from the hernia, and there tends to be relief. Belladonna may also give relief,

as well as a change in diet, with frequent small meals. One can, of course, have both conditions, — that is, angina pectoris and cardiospasm, — and not uncommonly one may excite the other. It is important to recognize this fact. Many patients with angina pectoris experience relief after belching, but the belching and the cardiospasm associated with it are secondarily induced by the attack of angina, or vice versa. The presence of both conditions adds to the difficulty of the diagnosis, but also to its interest.

Excessively severe chest pain occurring abruptly, — that is, within two or three seconds, — maximum at onset and radiating down the back, in a hypertensive person of middle age or older should suggest dissection of the aortic wall, that is, a dissecting aortic aneurysm. From the coronary-thrombosis group a few patients, as a rule hypertensives, can be picked whose aortic wall has split, usually along the whole length of the aorta and down into the iliaes.

The last point concerning pain has reference to right-upper-quadrant discomfort on effort, due to acute engorgement of the liver, in a patient with mitral stenosis or other cause of right-ventricular strain; this should be viewed with suspicion as an early, probably the earliest, symptom of failure of the right ventricle. Yet, even today, most doctors think of shortness of breath as being the first evidence of heart failure, even in the presence of mitral stenosis. Strictly, this is not true. To be sure, there is a defective mechanism whereby the increased shortness of breath, due to the pulmonary vascular congestion from mitral stenosis, may antedate actual failure. Mitral stenosis acts as a mechanical bar. With tachycardia due to effort, or coming paroxysmally, as in some cases of auricular fibrillation, the right ventricle pumps too much blood into the lungs; this causes congestion of the lungs and shortness of breath. Such dyspnea is due to overaction of the heart, not to heart-muscle failure.

The first symptomatic evidence of right-ventricular failure arises from engorgement of the liver. Naturally, just as the lungs fill up with blood when the left ventricle fails, with dyspnea as the first symptom, so swelling of the liver, with pain, is evidence of failure of the right ventricle. This may come on effort, just as shortness of breath may come on effort, but it is not as yet well recognized. Occasionally this clue is useful. Generally by the time right-heart failure is established, enlargement of the liver has become chronic and no longer painful, but the beginning of the congestion of the liver is painful. This symptom is worth looking for in patients with mitral stenosis who complain of

heaviness or discomfort, especially on effort, in the right upper quadrant of the abdomen. The liver can soak up blood rapidly, and it can also shrink extremely rapidly. I have seen enormous livers subside in forty-eight hours after the beginning of treatment. Thus failure of the right ventricle with a congested liver, like failure of the left ventricle with congested lungs, may subside quickly.

Dyspnea. When the heart is normal in size, dyspnea is not due to heart disease, that is, to either congestive failure of the left ventricle or mitral stenosis,—but most commonly to pulmonary disease or bronchial asthma. When such patients complain of dyspnea, digitalis should not be given. Hence it is extremely important in doubtful cases to determine the size of the heart. When it is normal, dyspnea must be related to other factors. There may be occasional exceptions,—cases of angina with asthmatic reflex,—but they are so rare that they seem to “prove the rule.”

In the presence of chronic hypertension of considerable degree, or myocardial infarction, new or old, or aortic valve disease, paroxysmal dyspnea, especially at night, is a bad sign, unless there is paroxysmal tachycardia, auricular fibrillation or severe pulmonary infection or infarction to set it off. It is evidence of acute failure (dilatation) of the left ventricle. Paroxysmal dyspnea has a much better prognosis in mitral stenosis. As stated previously, in mitral stenosis congestion of the lungs is not a sign of muscle failure; it is mechanical. I now have under my care a patient with mitral stenosis who ten years ago nearly succumbed to acute pulmonary edema caused by paroxysmal auricular fibrillation. She developed permanent auricular fibrillation and the heart rate has held ever since at about 70 under digitalis. The patient does not now have dyspnea, and remains in a fair state of health, an impossibility had she had left-ventricular failure as a cause of her pulmonary edema ten years ago. Cheyne-Stokes respiration in a patient when awake means serious circulatory failure. On the other hand, sighing respiration, like precordial tenderness, is a good sign, so far as the heart is concerned. If a patient heaves a deep sigh and says, “Well, here I am at last, Doctor,” one knows at once that the diagnosis is chiefly nervous fatigue, and can give, as a rule, a favorable prognosis. But a nervous person who sighs can also have angina pectoris, and nervous people can and do die of angina pectoris or coronary thrombosis.

Periodic dyspnea with tachycardia, collapse and fever, especially at rest, often means pulmonary embolism, particularly in a cardiac patient with congestive failure. This complication is impressive not only because of its importance and frequency,

but also because of its neglect. Many persons who are ill in a hospital or at home have unexplained attacks of dyspnea and prostration, and a slight elevation of temperature for a few days. Physical examination may fail to reveal pulmonary infarction, which is often hidden behind other signs; yet almost invariably embolism is responsible for such attacks.

It may be difficult to distinguish between paroxysmal tachycardia and pulmonary embolism. The pulse may go up to 150 or 160 in a few seconds or minutes. One suspects paroxysmal tachycardia, but then finds increased temperature, which is not caused by paroxysmal tachycardia or by heart failure alone—that is, when it amounts to more than half a degree or a degree. Therefore an elevation of two or three degrees of temperature for a few days after an unexplained attack of dyspnea or tachycardia is not to be attributed to either of these conditions. There is likely to be an infarction of the lungs. The embolus comes almost invariably from the legs. One often blames the heart, but in these cardiac cases especially there is a stagnation of blood in the veins of the legs. There may be no sign of phlebitis on physical examination in a good many cases. I have seen three or four of these patients with apparently perfectly normal legs but with proved thrombophlebitis (better called “phlebothrombosis”). There may be an incomplete block of one of the long veins, especially the superficial femoral or long saphenous, which is responsible for the pulmonary embolism that is causing the symptoms. One should be everlastingly on his guard against this complication. It may occur in a person who has never had heart disease. It is to be expected after an injury or an operation, but it is a common medical complaint as well.

One should in such cases always inquire as to possible injury. A recent patient, an elderly man, was suffering a second attack of so-called “pneumonia,” which was really a second pulmonary embolism. There had been no operation, and no swelling of the legs was present on examination. On inquiry, it developed that before the first attack of “pneumonia,” he was thrown across the room while wrestling, injuring his leg; he had had a temporary swelling of the ankle. Ten days later he had the second attack; the leg was responsible for the pulmonary embolism. Therefore inquiry should always be made as to possible injuries. One can save lives by ligating the responsible veins, when one is quite sure they are responsible. X-ray diodrast venograms, which are now possible, must be taken correctly. Not only is the technic important, but they must be interpreted accurately. Under such conditions they may reveal the correct cause of pulmonary embolism, which may have

been wrongly blamed on the heart. In that event one can tie off the veins on both sides. Lives can be saved by this procedure even more than by giving anticoagulants (such as heparin) after the phlebothrombosis has begun.

Palpitation. Palpitation as a preponderant or isolated symptom generally means an irritable or nervous heart, without structural disease. There need be no serious pain or dyspnea, but a good many nervous persons have every symptom, palpitation, shortness of breath, heartache, fatigue and faintness. The more symptoms, the less significant any one of them is when considered per se. Rarely palpitation does mean heart disease. The majority of long-lived persons throughout the world probably have occasional extrasystoles, of which they may or may not be conscious. Even auricular fibrillation may occur as a minor and isolated functional disorder. In over 100 cases I have seen auricular fibrillation as a relatively unimportant disorder with no other evidence of heart trouble; the hearts of these patients appeared to be structurally sound and essentially normal.

Premature beats, paroxysmal tachycardia and auricular fibrillation and flutter are the arrhythmias that are commonly the cause of palpitation, but still more commonly palpitation is merely an uncomfortable normal rhythm, fast, slow or average in rate.

Tachycardia in abnormal rhythms may explain pain without effort in coronary heart disease, congestive failure in cardiac strain and enlargement from any cause, even in normal infants, dyspnea in mitral stenosis from mechanical blocking of the pulmonary vessels with extra blood, and psychoneurosis, mild or severe, in patients who may become conditioned to any tachycardia. Arrhythmia and tachycardia may simulate coronary insufficiency. When an attack occurs at night, it is important to see the patient during it, or to get an accurate history of the attack. Tachycardia, which is difficult to control by digitalis and rest, particularly in auricular fibrillation, strongly suggests excessive nervousness, thyrotoxicosis, infection or infarction, especially of the lungs. If the heart cannot be adequately controlled in a cardiac patient one of these conditions is indicated.

Faintness and syncope are of more significance alone than when attended by other cardiac symptoms. If a patient faints and has other symptoms, such as palpitation and shortness of breath, neurocirculatory asthenia is the probable explanation.

SIGNS

With finger-clubbing, cyanosis means serious congenital heart disease, or severe chronic pulmonary disease, or is the result of prolonged residence

at altitudes of fifteen thousand feet or more. Cyanosis of high degree is rarely seen in congestive heart failure per se, and so when it appears in such cases, it should suggest a probable complication of pulmonary infarction or infection. Ayerza's disease (that occurring in so-called "black cardiacs") is more a pulmonary than a cardiac disease. The heart may be secondarily affected, with a large right ventricle, but failure of such hearts is seldom seen. The deep cyanosis in such cases is due primarily to the pulmonary disease. Cyanosis should be distinguished from argyria and polycythemia vera. The former occurs predominantly in the cheeks, tongue, ears and nose. Argyria occurs around the eyes and the sides of the nose and mouth. In a congenital cardiac patient, exercise increases the cyanosis, but in argyria it brings out a pinkness that tends to conceal the slate-blue tinge of the skin. Polycythemia gives a deep-red, rather than a purple color.

Jaundice in congestive failure suggests a large lung infarct superimposed on congestion of the liver, which is unable to take care of the blood pigment taken up from the pulmonary infarct.

Cardiac enlargement almost always means permanent heart disease, but there are a few exceptions, with acute and reversible dilatation, as in acute cor pulmonale, acute rheumatic myocarditis, excessive paroxysmal tachycardia, myxedema and some cases of myocardial infarction. One can distinguish preponderant left-ventricular and right-ventricular enlargement best by electrocardiograms, but total enlargement is best detected by x-ray study. A precordial bulge may be due to marked enlargement of the right ventricle.

As to sounds and murmurs, a greatly accentuated pulmonary second sound, especially one greater than the aortic sound, in hypertension means left-ventricular failure. In young persons without murmurs, it usually means congenital auricular septal defect or cor pulmonale; it is the rule in marked mitral stenosis. It is important to listen to the heart sounds. I attended medical school at a time when murmurs were all the rage and not much attention was paid to heart sounds. It was not realized that heart sounds were more significant than murmurs.

Gallop rhythm is almost always a sign of serious dilatation of the ventricles. One should, however, always rule out heart block.

Delicate aortic and mitral diastolic murmurs vary in audibility with body position, the type of stethoscopic chest piece and exercise. They are too often missed. In the interpretation of a continuous murmur, a venous hum in or transmitted from the neck should be ruled out; when that is done, such a murmur over the pulmonary-

valve area is the sign par excellence of patency of the ductus arteriosus.

A harsh systolic murmur at the apex, heard also at the aortic area but not over the lung bases, usually means aortic stenosis; when more blowing in character and heard also at the lung bases but not in the aortic area, a systolic murmur means mitral regurgitation. A systolic thrill palpable over the aortic valve area almost always means aortic stenosis, rarely an aneurysm; at the left border of the sternum it means as a rule a congenital ventricular septal defect.

Left versus right hydrothorax in heart disease is more often due to pulmonary infarction or pleurisy than to congestive heart failure. When hydrothorax is limited to the left side, it is due to some condition other than heart failure, unless the right pleural cavity is obliterated, because fluid usually collects earlier, and more frequently and more copiously in the right pleural cavity than in the left. If you find a limited hydrothorax on the left side, look out for pleurisy, pulmonary infarction or obliteration of the pleura on the right side. Also, look out for polyserositis. All fluid collections are not due to dropsy. There may be inflammation of the type of a polyserositis.

The same statement applies to the finding of rales at the lung bases; that is, pulmonary infection or infarction is the commonest cause of basal lung rales, or even atelectasis may be the cause, and not congestive heart failure.

Engorged neck veins almost always mean right-heart failure, rarely acute or chronic constrictive pericarditis or pressure from a mediastinal tumor, and they practically always mean that the liver is enlarged.

Enlargement of the liver without dilated neck veins and increased venous pressure indicates a noncardiac cause, such as cirrhosis in the early stage, hepatitis or tumor. The position of the liver edge is an unreliable indication of the size of the liver.

Exclusive or preponderant unilateral leg edema means local disease, even in heart failure, provided the effect of gravity—that is, of lying on one side—is ruled out. Often this disease is phlebothrombosis, which may lead to pulmonary embolism.

As to the pulse, a great difference in volume of wrist pulses suggests aortic aneurysm, but pressure from a cervical rib or a tight scalenus anticus muscle on one or the other subclavian artery may be responsible. A well-marked pulsus paradoxus favors acute or chronic constrictive pericarditis, but compression of subclavian arteries on raising the shoulders in deep inspiration should first be excluded. True pulsus alternans means serious left-ventricular weakness, except in cases of excessive paroxysmal tachycardia. Absence of pulse in the feet points oftenest to local occlusive arterial disease or embolism, dissecting aortic aneurysm or coarctation of the aorta. The deep systolic jugular pulse must not be confused with the carotid pulse. It should be recognized that there is a wide range of normal pulse rates in man.

* * *

In conclusion the examiner must everlastingly use his eyes and fingers, his ears and his brain in searching for these simple but important cardiovascular diagnostic clues; in fact, if he is on his toes, he may introduce some new and useful clues himself.

THE USE OF ETHER IN OIL INTRAMUSCULARLY IN
THE TREATMENT OF BRONCHIAL ASTHMA

ANGELO L. MAIETTA, M.D.*

WINCHESTER, MASSACHUSETTS

OLIVER WENDELL HOLMES spoke of his asthma as "the slight ailment that promotes longevity." Unfortunately, however, not all cases of bronchial asthma can be so described. Many cases are characterized by acute symptoms which, though severe, are not prolonged. In others, the asthmatic symptoms not infrequently become chronic and, with the passage of time, not only more intractable but also more severe. Quite often, during an acute episode, some patients pass into a more or less refractory stage during which their symptoms, despite energetic treatment, remain for a variable period constantly acute and relatively uninfluenced.

In the severely acute form, in intractable bronchial asthma (with or without acute seizure) and in status asthmaticus, I have found that the administration of ether in oil intramuscularly has produced gratifying results within a comparatively short time. I have successfully employed this preparation as an adjuvant form of palliative therapy in conjunction with other well-recognized and accepted methods. Its action has always been beneficial.

A report of the results obtained by treating 11 cases of bronchial asthma with intramuscular injections of ether in oil is herein presented. I fully appreciate that although ether in oil intramuscularly as an adjuvant appears to influence beneficially the asthmatic state of this small group of patients, much more clinical investigation is required for a more comprehensive evaluation of its effect.

MATERIAL

Ether in oil[†] can be obtained commercially in hermetically sealed ampules each containing 2 cc. of a sterile solution of equal parts, by volume, of anesthetic ether and peanut oil.

The administration of ether by injection is neither new nor rare. For years, ether has been classified as a diffusible stimulant¹ and recommended as a hypodermic medicament in its unadulterated state in doses of 15 to 20 minims, repeated in fifteen minutes if necessary.

In 1914, Audrain,² in France, introduced the intramuscular injection of ether as an anticonvul-

sant for the treatment of whooping cough in doses of 1 to 2 cc., repeated daily if required. In 1924, Mason,³ employing the same technic, was one of the first to introduce this therapy in America. Although the symptoms were favorably influenced, many American investigators thought that the treatment with crude ether hypodermically was not desirable because in a considerable number of cases pain, abscess formation and necrosis developed at the site of the injection. This serious objection was later overcome by diluting the ether with a bland oil (peanut oil) and keeping it aseptic in hermetically sealed ampules. In 1929, Levy and Finkelstein⁴ reported the use of this sterile ether in oil solution in 104 cases of whooping cough in which more than six hundred injections were administered without the occurrence of abscess formation or necrosis. The dose employed was 1 cc. of ether in 1 cc. of peanut oil, repeated on alternate days or daily as required. This is the same preparation of ether in oil that I have used for the treatment of bronchial asthma.

APPARENT MODE OF ACTION

There is ample evidence that ether, in some manner not as yet fully understood, has a modifying pharmacologic action on the asthmatic symptoms. According to Rackemann,⁵ ether in experimental anaphylaxis modifies anaphylactic shock so that the animal survives a dose of antigen that would otherwise be fatal. Vaughan⁶ states that asthmatic patients often experience relief for variable periods following surgery. This fact is well recognized by many allergists. Ether anesthesia was deliberately induced by Kahn⁷ in 4 patients with intractable asthma. They were temporarily relieved, but not for so long as sometimes happens after surgery. Since its introduction by Maytum,⁸ ether in oil by rectum for the relief of severe asthma has been well received by a number of investigators.

These facts have led to the intramuscular administration of ether in oil as an adjuvant for the treatment of severe bronchial asthma. Despite the fact that this method has had a limited employment, the results are so constant that an apparent mode of action may be rationalized.

Although the ether is mixed with peanut oil, the latter does not prevent the immediate diffusion of the ether because patients can taste and smell it within a few seconds following its introduction

*Associate professor of medicine, Middlesex University School of Medicine, Waltham, Massachusetts, physician-in-chief, Allergy Clinic, Middlesex Hospital, Cambridge, physician, Winchester Hospital, Winchester.

[†]Ether in oil is prepared by the Loeser Laboratory, Incorporated New York City.

into the body. On the other hand, the oil does materially prolong its volatilization and absorption, because patients are able to taste and smell it for twelve to twenty-four hours. From this it appears that absorption of the ether begins immediately but, owing to the oil, is prolonged, and that excretion occurs principally by the lungs.

It is probably because of the slow absorption of such a small dose that a slight depressing effect is maintained on the central nervous system. This depressing effect acts as an anticonvulsant and sedative and appears to influence favorably the bronchospasm and the patient's apprehension.

Also, because of the slow excretion of the ether by the lungs, tenacious mucus apparently is loosened and dislodged from the mucous membrane of the bronchial tree. Expectoration thus is facilitated. It is the difficult expectoration of this mucus, whether present in small or large amounts, that produces much distress because, owing in part to its foreign-body action, patients cough violently in an attempt to remove it. By loosening the mucus, its expectoration is accomplished more easily and quickly and less energy (coughing) is expended to expel it.

METHOD OF ADMINISTRATION

Ether in oil should always be injected intramuscularly, preferably in the gluteal or deltoid regions. Strict antiseptic precautions should be observed at all times. Immediately prior to the injection, the skin should be prepared antiseptically. For the injection, a 22-gauge intramuscular needle should be employed. Although a larger one permits a faster introduction of the material, this enhances the risk of rupturing a small blood vessel deep in the muscle tissue, which would allow seepage into the blood stream. Obviously, for this reason also, the injection should be made slowly, and after insertion of the needle the piston should be withdrawn slightly to ascertain the position of the needlepoint. If it is in a blood vessel the needle should be withdrawn and reinserted.

EFFECT OF INJECTIONS

When ether in oil is injected intramuscularly, the effects on an asthmatic patient may be described as immediate and delayed. The immediate effects are fleeting, occur within a few seconds, quickly disappear and are relatively unimportant. The delayed action of the preparation is apparently extremely beneficial, is usually evident in about two hours and may last from several hours to a week or several months.

Immediate effects. Immediately following the intramuscular injection of ether in oil, the patient is able to taste and smell ether from his breath.

This occurs within a few seconds to about three minutes and continues for twelve to twenty-four hours. Patients state that it is not unpleasant.

As soon as the needle is withdrawn, or even while administering the injection, most patients complain of slight to moderate, but not distressing, pain at the site of the injection. It has been described as a sharp, stabbing, burning or piercing type of pain, which disappears within a few minutes. No asthmatic patient thus treated has refused an intramuscular injection of ether in oil because of the slight pain it had produced in the past. At no time was there induration, edema, necrosis or abscess formation at the site of and as the result of the injection.

Following its administration, there is a slight increase in the pulse rate, usually about ten beats per minute. Its character remains unaltered. As a rule, the systolic blood pressure is slightly elevated (5 to 15 mm. of mercury). Occasionally the blood pressure may remain stationary or may even drop (about 10 mm.). The changes in both the pulse rate and blood pressure are transient, lasting about twenty minutes. These changes are undoubtedly due to the stimulating action of the ether. The patients, however, have not complained of palpitation and have experienced no ill effects.

About fifteen minutes after the injection, some patients occasionally have a slight feeling of dizziness and coldness of the extremities, particularly of the feet. The sensations disappear quickly, usually within a few minutes, and cause no alarm. These symptoms, more correctly described as side effects, are probably due to the odor of the ether that the patient obtains either while the injection is being prepared or, following the injection, from the taste. This mild side reaction is encountered in only a very few patients. In those in whom it occurs, it is no longer evident after the third or fourth injection.

Delayed effects. The therapeutic effects following the intramuscular injection of ether in oil become evident in about two hours. They are apparently due to the anticonvulsant and expectorant actions of the ether. Patients become quieter and breathe more easily. The ether also appears to have a favorable action on the bronchospasm. In cases in which epinephrine produces either partial or no relief, it again becomes effective if administered in one to three hours following the ether injection. Further, expectoration of tenacious mucus becomes easier. Whether the patient has "dry" asthma, with small amounts of a glistening, pearly material, or "moist" asthma, with large amounts of a thick, mucoid, yellowish-green substance, both types of which are difficult to expect-

torate, ether, excreted through the lungs, seems to hasten and facilitate the clearing of this substance from the bronchial tree. The elimination of this mechanical factor (tenacious mucus) immeasurably aids in terminating the attack.

DOSE AND RESULTS

Acute bronchial asthma Of the three clinical groups considered here—acute bronchial asthma, chronic bronchial asthma and status asthmaticus—the first is the least important because, in an uncomplicated case, sooner or later the symptoms respond to the usual medications. However, there are patients who respond favorably but not completely and in whom palliative medication must be continued for several days until relief is obtained. In such cases, an intramuscular injection of ether in oil, repeated in four to six or twelve hours if necessary, appears not only to aid the symptoms but also to render epinephrine and ephedrine more efficacious. One or two injections are usually sufficient.

Six patients, having had an attack of acute asthma from two to five days, were thus treated. All of them responded fairly well but not satisfactorily to injections of epinephrine, 1/1000, and to a combination of 1/2 gr of ephedrine sulfate, 2 gr of aminophyllin and 1/4 gr of phenobarbital, given by mouth. Four of them received one intramuscular injection of ether in oil, the remaining 2 received two each. Within two hours, the asthmatic symptoms were rapidly controlled. The patients became quieter, were able to breathe more easily and expectorated more freely. Thereafter, the usual palliative medications effectively controlled the symptoms.

Chronic bronchial asthma Patients in this group have usually had their asthma for years, some as long as thirty or forty years. They generally have asthma the year around and suffer many acute exacerbations. Some of them have developed emphysema, with or without a barrel-shaped chest, and in some a minimal amount of tubular or sacular bronchiectasis is present. These patients are constantly raising a thick, mucoid or yellowish green substance. Its removal by coughing often produces much distress and aggravation of the symptoms.

In this group, ether in oil intramuscularly is extremely beneficial. Its administration renders expectoration much easier. The patients thus become more comfortable and, as the mucus and cough diminish, may even become symptom free unless there are marked secondary changes (emphysema and bronchiectasis) or a fresh episode is encountered. The beneficial results may last for several months or longer.

The dose is usually one or sometimes two injections per week, and may be continued in conjunction with other approved treatment until the cough, wheezes and sputum are reduced to a minimum. It cannot be emphasized too strongly that intramuscular ether in oil is an adjuvant and that it is not intended to replace other therapeutic agents.

Three cases of chronic bronchial asthma were so treated. Expectoration increased considerably and, after four or five injections, the symptoms were markedly improved. In these cases, the administration of ether in oil was continued weekly for about three months.

Status asthmaticus This disease presents a most distressing clinical picture. The patients are in a state of constantly acute asthma and do not respond appreciably to medication. They are referred to as adrenalin fast cases. In these cases intramuscular ether in oil appears to be an excellent adjuvant. In about two or three hours following its administration, beneficial results may be noted. The patients become quieter, expectorate more freely and profusely, and other palliative medications become more effective. The dose, one ampule, should be repeated every four to six hours as indicated by the response and progress of the patient.

Two patients with status asthmaticus were treated. One received nine intramuscular injections of ether in oil, the other eleven. Although both these patients had chronic asthma and had never been completely free of their symptoms, one has remained symptom free for more than four months, and the other for more than six months.

SUMMARY

Ether in oil intramuscularly as an adjuvant for the treatment of bronchial asthma is suggested.

It appears to act as an anticonvulsant and expectorant, thus beneficially influencing the asthmatic state.

The good results obtained may last from several hours to several weeks or months and justify further clinical studies.

409 Main Street

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CLINICAL NOTE

SUCCESSFUL POST-MORTEM
CESAREAN SECTION

REPORT OF A CASE

RICHARD J. MORAN, M.D.*

CAMBRIDGE, MASSACHUSETTS

BECAUSE of the relative rarity of cases of successful post-mortem cesarean section, in the medical literature,¹⁻³ it is thought worth while to report the following case:

CASE REPORT

H. M., a 24-year-old gravida III para I, entered the Cambridge City Hospital on January 19, 1941, with a chief complaint of cough and difficult respirations. Three days previously she had noted onset of cough, sore throat, generalized muscle aches and low-back pain, together with dyspnea. These symptoms all regressed except the cough and dyspnea, which had grown steadily worse. The cough was productive of thick yellow sputum. The patient had had no chill, chest pain or hemoptysis. She was seen by her family physician, who advised hospitalization.

The patient had had bronchial asthma for the preceding 8 years without treatment. She had one living child, 3 years of age. Her second pregnancy had resulted in a stillbirth. Her last menstrual period occurred about June 20, 1940, so that on entry she was slightly less than 7 months in gestation. The prenatal care had been adequate. She was first seen on October 30, 1940, with a blood pressure of 90/60; it was noted that she was nervous and apprehensive. On December 11 the blood pressure had risen to 136/70. She had gained 9 pounds, her weight at that time being 228 pounds. She was seen on January 8, 1941, and had no toxic signs or symptoms; the blood pressure was 152/76, and the body weight 232 pounds. She was not seen again until the day of admission.

Physical examination revealed a well-developed, obese white woman lying propped up in bed, wheezing and coughing. The temperature was 100.4°F., the pulse 134, and the respirations 36. Both lung fields were diffusely filled with fine moist expiratory rales. Occasional coarse inspiratory rales were heard over the bases posteriorly. Expiration was prolonged. The abdomen was obese, and there was a midline tumor mass extending two thirds of the way to the ensiform cartilage. The fetal heart was audible in the right paraumbilical region and was regular. The diagnoses at that time were seven-month pregnancy, bronchial asthma and grippe.

The patient was immediately given adrenalin, intravenous aminophyllin, calcium gluconate and 50 cc. of

50 per cent glucose intravenously, but respiratory distress continued. She was put into an oxygen tent. A portable chest plate was taken, the report being: "Mottled areas of increased density scattered throughout both lung fields. The appearance is consistent with an extensive bilateral bronchopneumonia." Sputum typing and blood culture were immediately done, and both were reported positive for Type 3 pneumococcus. Type 3 rabbit serum was obtained from the Massachusetts Department of Public Health, and the patient was skin-tested. The reaction was markedly positive to a 1:1000 dilution, and an ophthalmic test was positive to a 1:100 dilution. Advice was sought from Dr. Maxwell Finland of the Pneumonia Service of the Boston City Hospital. He emphatically advised that serum should not be given, and it was therefore withheld. Sulfathiazole was given in full therapeutic dosage.

On the morning of the 4th hospital day the patient was seen by the Obstetrical Service. They advised discontinuing the pregnancy and treating the pneumonia, but added that in the event of death a post-mortem section should be considered. On the same day the patient rapidly became worse. The temperature rose to 105°F., and the pulse was over 160. The color remained good,—in the oxygen tent,—but the patient became comatose at about 11 p.m. Coarse moist rales were audible throughout both sides of the chest, and the fetal heart could not be heard in the presence of the loud gurgling respirations.

In spite of constant and energetic measures to restore the patient, she failed to rally, and preparations were hastily made for a post-mortem cesarean section. Terminally the respirations became short gasps with long intervals of apnea. The oxygen tent was kept going continuously, and the patient's color remained good. She was pronounced dead at 3:24 a.m., no fetal heart sounds having been heard for about 4½ hours. About 20 seconds later the abdomen was opened by a single midline incision, and the uterus sagged forward. The fundus was opened, and the baby was delivered manually. A small incision was inflicted on the baby's right cheek by accident when the uterus was opened. Alpha-lobeline was injected into the umbilical cord, which was apparently pulseless, and within a few seconds respirations were established. The infant, a female, was transferred to an incubator, and given oxygen as needed. Vitamin K was given and gavage feeding was begun within 24 hours. The early feeding consisted of water, glucose and whisky, later supplemented by breast milk.

At birth the infant weighed 3 pounds, 6 ounces. After an initial loss of 2 ounces in weight she made uneventful progress. She left the hospital after 7 weeks, weighing 6 pounds, and is at present in good health.

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*Formerly, intern, Cambridge City Hospital.

MEDICAL PROGRESS

THE SULFONAMIDES**

I. Their Mode of Action and Pharmacology

CHARLES A. JANEWAY, M.D.†

BOSTON

IT IS six years since Prontosil, synthesized by Mietzsch and Klarer¹ and proved to be effective against the hemolytic streptococcus in mice by Domagk,² first came to the attention of the English speaking medical world as a potent chemotherapeutic agent in man, with Colebrook and Kenny's³ report on its use in puerperal sepsis. There have been few more important medical discoveries, and it can be truthfully stated that the introduction of the sulfonamide drugs marked the beginning of a new era in medicine. Bacterial infections, most of which had been treated by purely symptomatic measures, suddenly became amenable to therapy, and the reduction in the mortality of such severe infections as hemolytic streptococcus meningitis, pneumococcal pneumonia and meningococcal meningitis has been little short of miraculous.

It is small wonder that there has been a flood of papers on the use of the sulfonamides or that those in practice have been somewhat confused by the rapidity with which the popularity of one new sulfonamide derivative after another has waxed and waned. The only justification for adding this report to the multitudes already written is that I have been struck by the need for a very concise and practical presentation of the present state of our knowledge of these drugs.† In this and the following article, an attempt will be made to summarize what has been learned in six years about their usefulness and limitations and to put this information in such a form that it will be helpful to those who are called on to use the sulfonamides in everyday practice. This type of presentation must necessarily be somewhat dogmatic. Since the sulfonamides play such an important role in both civilian and military medicine, the times will justify the repetition in condensed form of what

can be found in the writings of many workers in the field of chemotherapy.

MODE OF ACTION

The intelligent use of these drugs presupposes an understanding of their mode of action. *There is overwhelming evidence that they act on the organisms to delay or completely to inhibit their multiplication and do not increase the defensive powers of the host.*

Resistance to pyogenic infections depends on the speed and intensity of the inflammatory reaction, which localizes the infection nonspecifically, and on the presence of specific antibody, which makes possible the destruction of organisms by phagocytosis or lysis. There is no evidence that the sulfonamide drugs act through either of these mechanisms. Nonspecific inflammatory localization is promoted by the time honored measures of heat and rest, the former to increase circulation to the inflamed area, the latter to keep the drainage of lymph at a minimum and to allow minute thrombi to form about the focus in lymphatics and capillaries. Specific antibody may be administered when it is lacking, as in the serum treatment of pneumonia.

The virulence of pathogenic organisms, however, depends not only on their ability to secrete substances that inhibit inflammatory localization, such as streptococcal fibrinolysin, and their ability to escape destruction by the phagocytes in the early stages of infection, but also and above all on their ability to multiply in the tissues of the host. This property is fundamental to all pathogens, and the most invasive bacteria, such as those of anthrax and plague, are able to utilize the substances in the body fluids of the host so effectively that they multiply at an astonishing rate and overwhelm their victim. The sulfonamides attack this aspect of virulence. If a sufficient concentration of a sulfonamide drug is added to a tube of culture medium, the growth of susceptible organisms is inhibited. If sufficient concentration of a sulfonamide is present in the body fluids of the patient, these fluids become poor mediums for the growth of many species of micro-organisms, and thus infections with these organisms may be brought under control, by what amounts to a process of starvation of the

Reprints of articles in this series are not available for sale but on request the articles will be published in book form. The current volume is *Medical Progress Annual Vol. III 1942* (Springfield, Ill. no. 3 Charles C. Thomas Company 1942 \$5.00).

*From the Medical Clinic, Peter Bent Brigham Hospital and the Department of Medicine and of Bacteriology and Immunology, Harvard Medical School.

†Assistant Professor of Pediatrics, Harvard Medical School, and Physician, Children's Hospital, associated in medicine, Peter Bent Brigham Hospital.

There is one excellent manual which every practicing physician would do well to own. *Guide to Therapy for Medical Officers*, War Department Technical Manual 8-210 obtainable from the United States Government Printing Office, Washington, D. C., for 25 cents. Section V (pages 110-113) covers sulfonamide chemotherapy briefly and accurately.

bacteria. However, the organisms are often only starved into submission, and their release from the inhibitory activity of the sulfonamide before the body's defenses have been able to localize them or destroy them, or before the bacteria have autolyzed, is followed by rapid multiplication and the return of signs of infection.

The most important observation on the mode of action of these drugs was the finding by a number of workers⁴⁻⁷ that there are substances capable of inhibiting the bacteriostatic action of the sulfonamides. The only inhibitor substances that have been identified chemically are para-aminobenzoic acid and its esters, among which is procaine. These substances have been found in killed and autolyzed bacteria,⁵⁻⁷ yeast,⁸ autolyzed liver, pus and other tissue-breakdown products.^{9, 10} MacLeod's demonstration of the presence of sulfonamide inhibitor in pus and of its absence from serum explains the marked difference in therapeutic response between rapidly spreading infections such as pneumonia and localized purulent foci such as empyema.¹¹ It is a point of great theoretical interest that just as only the para-form of aminobenzene-sulfonamide is effective against bacteria, whereas the meta-isomers and ortho-isomers are relatively inert, so the para-form of aminobenzoic acid alone of its isomers possesses the ability to inhibit sulfonamide action.⁸

In vitro study of the effect of sulfonamides on bacterial growth has shown that the curves have the character depicted in Figure 1. At first, in the period A-B, growth takes place at the normal rate. This is known as the "lag" phase. At B some change occurs, and from B to C is the period of *bacteriostasis*. Under proper conditions the population may fall in the period C-D, and the bacteriostatic effect can be said to have been sufficient to become *bactericidal* (Curve 1). Under other conditions the events depicted by Curve 2 may occur, and there is a phase of "escape."

Two mechanisms may make this escape possible. Enough organisms may autolyze to liberate sufficient inhibitor substance into the medium to overcome the sulfonamide effect, or drug-resistant organisms may develop, capable of growing in the presence of the drug. Such drug-fast strains can be produced by passing organisms through mediums containing increasing concentrations of the drug.¹²⁻¹⁴ That drug-fastness depends on the ability to synthesize more para-aminobenzoic acid is suggested by the observation that drug resistance does not develop in the presence of small amounts of the acid^{13, 15} and by the studies of Mirick,¹⁶ which showed that a drug-resistant pneumococcus synthesizes ten times as much para-aminobenzoic

acid as its parent strain. In actual clinical practice, the development of sulfonamide resistance has been

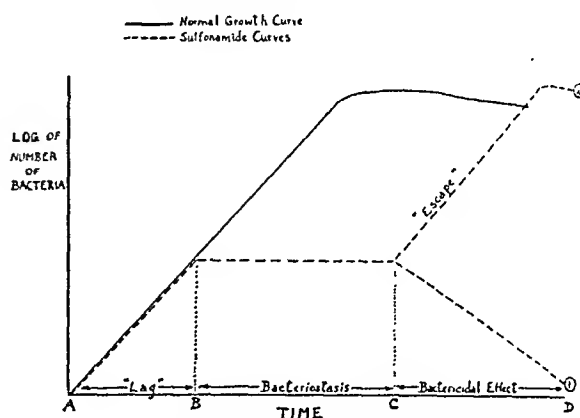


FIGURE 1. Schematic Representation of Normal Growth Curve of a Micro-Organism and Its Growth Curve in the Same Medium Containing an Effective Concentration of a Sulfonamide Drug.

observed only a few times,^{15, 17, 18} but the fact that it may develop is an argument for treating infections intensively at the beginning.

The lag phase corresponds to the clinical observation that there is a period of several hours after chemotherapy is begun before a therapeutic effect is noticeable. This suggests that some change must occur either in the bacteria or medium during this period. There is proof that this change involves the organisms and not the medium, and that it is readily reversible.^{19, 20} Recently Rose and Fox²¹ have suggested that it is due to the exhaustion of a substance present in the parent bacteria, which cannot be synthesized by the bacteria in the presence of sulfonamide. Their evidence for this is that, at the minimal effective sulfonamide concentration, the bacteria divide only a fixed number of times before inhibition of growth occurs, no matter what the size of the inoculum or the character of the medium, provided it does not contain para-aminobenzoic acid.

In 1940, Fildes²² propounded his theory that the sulfonamides and other antibacterial substances act by interfering with the metabolism of an essential metabolite ("an organic substance without which metabolism cannot proceed to the extent required by growth"). Since that time a series of papers from his laboratory have built up a convincing array of evidence for this hypothesis, and have placed the further development of sulfonamide therapy on a rational rather than an empirical basis.

Woods⁸ identified para-aminobenzoic acid as the specific inhibitor of the action of the known sul-

fonamides. From his work, he suggested that sulfanilamide, by virtue of its chemical similarity to para-aminobenzoic acid, replaces the latter as the substrate for an enzyme concerned with the further utilization of this essential metabolite. Whether or not bacteriostasis or growth occurred in such a system, depends on the relative proportion of the two competing substrates. If the proportion of para-aminobenzoic acid to sulfanilamide was more than 1:5000, growth occurred; if less, growth did not, regardless of the absolute concentrations of either substance. Such a theory of competitive inhibition still does not explain why the critical ratio of para-aminobenzoic acid to sulfanilamide is 1:5000 with a given strain of micro-organism whereas the ratio of para-aminobenzoic acid to sulfathiazole with the same strain is 1:3, but it explains all other known facts very well. A partial explanation, at least, for the differences in bacteriostatic efficiency of the various sulfonamide drugs has been offered by Fox and Rose.²¹ They found that the critical ratio of para-aminobenzoic acid to sulfonamide was much more nearly the same for the different drugs if only the concentration of ionized sulfonamide was considered. Schmelkes and his co-workers²⁴ have come to the conclusion that the active sulfonamide exists as an anion, and recently Cowles²⁵ has reported evidence further strengthening the hypothesis that ionization plays a decisive role in sulfonamide action.

One necessary assumption is that para-aminobenzoic acid is an essential metabolite for bacteria. Evidence for this has been provided by Park and Wood,²⁰ who showed that, in the presence of biotin, extremely minute amounts of para-aminobenzoic acid produced a marked stimulation of growth of *Clostridium acetobutyricum*. A practical application of the identification of para-aminobenzoic acid as a specific inhibitor of the bacteriostatic action of the sulfonamides is its inclusion in culture mediums so that organisms present in the blood and other body fluids of patients under sulfonamide therapy will grow at a normal rate.²⁷

On the basis of Fildes's general theory and Woods's elaboration of it for the sulfonamides, it should be possible, from a knowledge of bacterial metabolism, to prepare chemotherapeutic agents which will inhibit the utilization of other essential metabolites. The validity of the hypothesis has been tested and supported in experiments conducted by Fildes's associates. By replacing a carboxyl group on an essential metabolite with a sulfonic group, the utilization of the metabolite may be competitively blocked by a sufficient concentration of the new and unnatural, but chem-

ically similar compound. A list of those compounds already tried follows:

AUTHOR	ESSENTIAL METABOLITE	GROWTH-INHIBITOR
Woods ⁸	Para-aminobenzoic acid	Sulfonamides
McIlwain ²⁸	Nicotinic acid	Pyridine-3-sulfonic acid
McIlwain ²⁸	Nicotinamide	Pyridine-3-sulfonamide
McIlwain ²⁹	Alpha-amino-RCOOH	Alpha-amino-RSO ₃ H
McIlwain ³⁰	Pantothenic acid	Pantoyl taurine
Fildes ³¹	Indole; tryptophan	Indolacrylic acid

McIlwain³⁰ has proposed what he has called the antibacterial index for characterizing such systems. This is the ratio of the minimal effective concentration of the bacteriostatic agent to the concentration of the corresponding metabolite. Such a ratio is constant for any particular organism, although the absolute amounts of the two substances may vary over a wide range. The determination of such ratios, of course, involves the use of synthetic culture mediums of known composition, so that the concentrations of the substances being tested can be accurately measured. From a knowledge of such a ratio, of the concentration of the essential metabolite in tissue fluids and of the toxicity and absorption of the bacteriostatic substance, it should be possible to determine whether or not a new chemotherapeutic agent of this type can be expected to work in vivo against a particular organism.

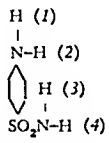
Thus, in seven years, chemotherapy has progressed from the more or less empirical discovery of an azo-dye, Prontosil, to the synthesis of new chemotherapeutic agents which can be designed to attack the most vulnerable facet of an organism's metabolism. It should not be forgotten that none of this progress would have been possible had not the laborious work of elaborating the growth requirements of bacteria been going on for many years. It is largely due to the work of men like Fildes in England and Mueller in this country that the science of bacteriology has been carried forward to the point where it can provide the tools for the further development not only of the field of chemotherapy, but of human nutrition as well.

PHARMACOLOGY OF SULFONAMIDE DRUGS

Besides an understanding of the way in which the sulfonamides act on bacterial infections, it is essential for a physician who uses these drugs to have accurate knowledge of their pharmacology. When drugs such as aspirin are used for the relief of symptoms, little more knowledge than the average layman possesses is necessary, but when poten-

tially dangerous remedies are used in large doses for the treatment of serious diseases, detailed pharmacologic knowledge is as vital to the physician as are a knowledge of anatomy and a skilled technic to the surgeon performing a difficult operation.

The pharmacology of these drugs can best be presented in tabular form after a few general remarks. All the sulfonamides in common use are derivatives of sulfanilamide, which has this formula:



The numbers after the hydrogen atoms are to identify them for convenience in the text.

Two types of sulfanilamide derivative have come into clinical use. The first type involves a replacement of hydrogen atom (4) by some nucleus, from which the compound derives its name. Thus, sulfapyridine consists of sulfanilamide with hydrogen (4) replaced by the pyridine ring. These com-

side of the vein. However, at 0.5 per cent strength they may be used subcutaneously in infusions.* *They must never be used intrathecally, as their alkalinity will produce irreparable damage to the nervous tissue.*

A second type of sulfanilamide derivative has been introduced by Marshall and his associates³² as a result of their studies of sulfaguanidine, which was synthesized by Roblin and his co-workers. Sulfaguanidine is water-soluble to a considerable degree, but is absorbed very poorly from the bowel, so that high concentrations of the drug in the intestinal tract may be achieved while the blood level remains low. While sulfaguanidine involves a substitution of a guanidine radical for hydrogen atom (4), succinyl sulfathiazole, which is now being tested for its effect in the bowel, has a succinic acid chain coupled to the para-amino group replacing hydrogen (2). In the bowel the succinic acid is split off, liberating sulfathiazole, which is more potent than sulfaguanidine and is comparatively little absorbed in the large intestine.³³

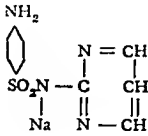
The present knowledge of the distribution of these drugs is the result of the development of ac-

TABLE 1. Characteristics of the Sulfonamide Drugs.*

DRUG	RATE OF ABSORPTION	DEGREE OF CONJUGATION	RATE OF EXCRETION		DESIRED BLOOD LEVEL	SURJECTIVE DISCOMFORT	INCIDENCE OF COMMON TOXIC SYMPTOMS			
			FREE	CONJUGATED			NAUSEA AND VOMITING	ACUTE HEMOLYTIC ANEMIA	BUILD ANEMIA	GRANULOCYTOPENIA %
Sulfanilamide	Rapid	Usually about one third	Rapid	Fairly rapid (soluble)	8-15	Very frequent	Frequent	Fairly frequent (2-3%)	Almost constant	<1
Sulfapyridine	Irregular	Usually high	Moderately rapid	Slow (moderately insoluble)	5-10	Frequent	Very frequent	Rare	Frequent	<1
Sulfathiazole	Rapid	Usually less than one third	Very rapid	Rapid (very insoluble)	3-7	Rare	Frequent	Very rare	Rare	<2
sulfadiazine	Fairly slow	Usually less than one third	Slow	Moderately slow (soluble)	8-15	Very rare	Rare	Rare	Moderately rare	<1

*Percentages where used are from Long's³³ published statistics.

pounds are all more potent than sulfanilamide. However, they are much less soluble, and for that reason they are unsuited for parenteral use. The substitution of a sodium atom for hydrogen atom (3) renders them soluble in high concentrations and they may be injected intravenously as 5 per cent solutions in distilled water or saline solution. Thus the formula for sodium sulfadiazine is:



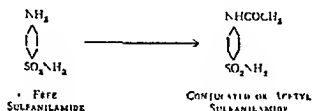
These sodium salts are quite alkaline and are extremely irritating if injected into the tissues out-

curate methods for their estimation by Fuller³⁴ in England and by Marshall and his co-workers³⁵ in this country. The method depends on the fact that sulfanilamide or its derivatives when coupled to N-(1-naphthyl)-diethyleneamine develops a purple-red color. This reaction is specific for the para-amino group and is accurate except in the presence of procaine, which is an ester of para-aminobenzoic acid. If, for example, novocain is allowed to enter the pleural cavity in preparation for thoracentesis, the fluid removed may appear to contain much larger amounts of sulfonamide than it actually does.

The important facts that should be known about each sulfonamide are its rate of absorption

*There is recent evidence that concentrations as high as 2 per cent are tolerated on subcutaneous injection

and rate of elimination, since on the balance between these depends the level achieved. Absorption of the substituted sulfonamide takes place mainly in the stomach. It is modified by food, and is most rapid before meals but most complete after meals.³⁶ Alkali may play a role in increasing the amount absorbed. Elimination may occur in two ways, either by excretion of the unchanged or free drug in the urine or by conjugation of the free drug to a combined form, probably in the liver. The conjugated form, which has little therapeutic activity, is excreted in the urine also.



The determination of the amount of conjugated sulfonamide present is made by determining the free drug in the usual manner, then hydrolyzing the sample with heat and acid for one hour, which

Toxic effects follow a general pattern for the whole group, with some differences between individual drugs.

Nervous symptoms are always present to greater or less degree, and usually appear soon after therapy is begun. These vary from mild lassitude or anorexia through nausea and vomiting to frank psychosis. Nausea and vomiting are listed as nervous, since they are clearly central in origin. The mechanism of these symptoms is not yet clearly understood, although it has been suggested that they represent subjective reflections of disturbances in metabolism of nervous tissue produced by the drug. In any case, acute poisoning of animals with large doses of the sulfonamides results in convulsions and spasticity, evidences that the central nervous system has suffered most severely. Various vitamin preparations, particularly nicotinic acid, and oxygen have been recommended for their control, with different results in the hands of different investigators. The advent of sulfadiazine, which produces very little subjective disturbance, has made such accessory therapy unnecessary. An important practical point is that an ambulatory patient taking sulfonamides should be warned that his reaction time may be slowed. Special care should be observed in driving a car, crossing streets and performing manual work.

*Acidosis** occurs only when sulfanilamide is used, since it is associated with inactivation of the enzyme, car-

TABLE 1 (continued).

INCIDENCE OF HYPERSENSITIVITY RASH	TENDENCY TO SENSITIZE	INCIDENCE OF RENAL COMPLICATIONS	COMMENT
%			
1 Frequent (10%)	Moderate	Very rare	Seldom used because of subjective discomfort, low potency and anemia
2 Fairly frequent (4%)	Slight	Hematuria, fre- quent, oliguria, occasional	Potent, but seldom used because of vomiting and irregular absorption
5 Very frequent (10% or more)	Marked	Hematuria occa- sional oliguria, frequent	Very potent and well tolerated but most apt to cause renal complications and to sensitize, causing rash and fever on subsequent administration. Difficult to maintain desired red blood level because of rapid excretion.
2 Moderately rare (2%)	Slight	Hematuria, occa- sional, oliguria, rare	Not quite so potent, but best tolerated and high blood levels easily achieved because of slow excretion. Treacherous since serious toxic reactions may occur after cessation of therapy, also owing to slow excretion.

converts the conjugated to the free form, and re-determining the amount of drug.

The distribution of these drugs within the body varies considerably. This may depend in part on differences in ionization already mentioned, but even more on the binding of the different drugs by the proteins of the plasma, as demonstrated by Davis.³⁷ At one extreme, sulfanilamide appears to traverse membranes with little difficulty and is found in the red cells and in the spinal fluid in concentrations similar to those in plasma, whereas at the other extreme, sulfathiazole remains chiefly in the plasma, appearing in both red cells and spinal fluid in considerably lower concentrations. In most inflammatory exudates, these drugs are found in concentrations closely approximating those of the blood.

Loume anhydrase. This inactivation has been shown to be due to the sulfonamide group and not to the para amino group on which antibacterial activity depends.^{39, 40} In the substituted sulfonamides the sulfonamide group is covered by the substituent nucleus, and thus cannot react with the enzyme. Bicarbonate of soda diminishes acidosis with sulfanilamide, but is not necessary with the other drugs.

Cyanosis, so prominent and insightfully a manifestation of sulfanilamide therapy, is slight with the other drugs. It has been proved to be due to a combination of methemoglobin⁴¹ and the colored oxidation products of sulfanilamide, some of which are responsible for the oxidation of hemoglobin methemoglobin.⁴² It can be reversed by the reducing action of methylene blue,⁴³ but usually does no harm. However, the production of methemoglobin by

*This acidosis is characterized by a loss of sodium ions in the urine and a reduction of the bicarbonate and sodium ions and an increase of the chloride ions in the plasma. With this clinical picture, hyperventilation develops. These changes are reversed when the drug is stopped.³⁸ Bicarbonate of soda acts on it as a symptomatic remedy that relieves the hyperventilation to some extent.

sulfonamide therapy is of possible importance in aviation medicine. Methemoglobin will not carry oxygen, and aviators undergoing chemotherapy should suffer from anoxia at lower altitudes than normal men. Since anoxia is one of the chief limiting factors in aerial combat, these men should be grounded until they are well.

Blood disturbances are all too common and may assume almost any form. Acute hemolytic anemia, which may be severe enough to cause hemoglobinuria, is rare except with sulfanilamide. It generally comes on in the first few days of therapy. This type of anemia can be produced by many chemically related substances, notably para-aminophenol,⁴⁴ which may possibly be produced in vivo from sulfanilamide. Low-grade anemia, which may be remedied by transfusion, is a common accompaniment of prolonged sulfonamide therapy. The granulocytes are particularly sensitive to many compounds derived from benzene, and therefore agranulocytosis and granulocytopenia may occur with all these drugs. Thrombocytopenia, with purpura, likewise has been described with all the drugs in common use, although it is extremely rare.

Skin manifestations are manifold. Various types of erythematous eruptions—particularly morbilliform or nodose—have been observed. A few cases of exfoliative dermatitis have followed sulfonamide therapy. These rashes frequently accompany fever, lymphadenopathy, splenomegaly and arthralgia, to form a picture quite comparable to serum sickness. Furthermore, these toxic reactions occur most frequently from the fifth to the fifteenth day after the beginning of therapy, and if a patient once has such a reaction, the readministration of a small dose of the drug will suffice to precipitate the reaction in the space of a few hours. This phenomenon is analogous to that of accelerated serum sickness.

Fever is one of the commonest and most confusing toxic reactions, especially when it occurs without rash, arthralgia or lymphadenopathy. Its mechanism is not understood any better than that of other drug sensitivities, such as the ninth-day erythema of arsphenamine treatment, to which it is entirely comparable. As yet nobody has been able to demonstrate the presence of specific antibodies in patients who develop this form of hypersensitivity. An attempt to transfer hypersensitivity passively to normal people with the serum of the most sensitive patient observed was entirely unsuccessful.⁴⁵

Visceral damage may occur in sulfonamide therapy. Hepatitis with jaundice has been reported, but it is very rare. Renal damage simulating the nephrosis of bichloride poisoning may occur with rather small doses of sulfathiazole and probably represents a true toxic nephritis.⁴⁶ Myocardial lesions occur pathologically in patients receiving sulfathiazole, and intraventricular block has been observed in a patient with severe intoxication.^{45, 47} One or two cases of encephalopathy from sulfathiazole have been reported, and are possibly analogous to the hemorrhagic type of encephalitis, which is a rare but very severe form of intoxication with the organic arsenicals.

Oliguria due to precipitation of the drug has been observed only with the relatively insoluble substituted sulfonamides and not with sulfanilamide, which has a relatively high degree of solubility. As the glomerular fil-

trate passes down the renal tubules, it is concentrated by the resorption of water. This may result in a concentration of the urine to a point where the solubility of the sulfonamide or its acetylated form is exceeded and precipitation occurs.* Hematuria, calculus formation or tubular obstruction may result, with consequent oliguria and eventual renal shutdown unless something is done quickly to prevent it.

That sulfonamide therapy produces not only functional and chemical disturbances in the patient, but morphological changes as well, has recently been conclusively proved. A number of authors⁴⁸⁻⁴⁹ have described multiple small nodules of miliary necrosis in the tissues of patients receiving sulfathiazole. Rich,⁴⁹ in an investigation of the pathology of serum sickness, has described lesions indistinguishable from those of periarteritis nodosa. It is significant that most of his patients had received sulfonamides as well as serum and that he found similar lesions not only in a case of serum sickness before the days of chemotherapy, but also in a patient who had received nothing but sulfathiazole. If this finding can be substantiated, it will provide pathological evidence for the essential similarity between the hypersensitivity developing as a result of sulfonamide administration and that following foreign serum.

The pharmacologic properties of the individual sulfonamide drugs are assembled in Table I in such a way that they are readily available for the physician who must choose which drug he will use. When the individual drugs are compared, certain differences between them do stand out clearly. Sulfanilamide is conspicuous for the frequency of cyanosis, acidosis and acute hemolytic anemia. Sulfapyridine is characterized by two outstanding properties—its tendency to produce nausea and vomiting and its antipyretic action.^{50, 51} Of all the drugs in this group it is the only one which is antipyretic, and thus temperature is not a reliable criterion for control of infection with sulfapyridine. Sulfathiazole and sulfadiazine are both remarkably well tolerated by most patients. However, there is increasing evidence that sulfathiazole is a fairly toxic drug, and unfortunately, sulfadiazine, although it produces severe reactions less frequently, is treacherous because of its slow excretion.

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*Bicarbonate of soda has been recommended to make the urine more alkaline and thus prevent crystal deposition. It is doubtful whether the urine can be rendered sufficiently alkaline to alter markedly the solubility of these compounds. Soda may be given when hematuria or oliguria occurs, but its routine administration is not justified, because these patients already have to take so many pills.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28521

PRESENTATION OF CASE

First admission. A twenty-three-year-old single English typist was admitted because of chronic productive cough of thirteen years' duration.

Nineteen years prior to admission the patient suffered with a severe attack of whooping cough. The cough persisted for a year and finally cleared up spontaneously at a seashore resort. During the succeeding seven years she had recurrent colds, sore throats and several episodes of "draining ears." Her "tonsils and adenoids were snipped" several times, and following the last tonsillectomy twelve years ago, she developed a chronic cough. During the next ten years the cough gradually became severer and more productive so that at the time of admission she raised half to three quarters of a glassful of foul-smelling greenish sputum each day. The greatest amount was raised in the morning and in the evening on return from work. The patient had recently noticed blood streaking of the sputum, and at times she expectorated large tenacious plugs. She attempted postural drainage, but this proved too strenuous for her.

Four years before entry many nasal polyps were removed. Two years previously a radical antrum drainage was established without improvement. At that time, she suddenly developed severe sharp pain in the left chest. Her physician believed that she had pleurisy and accordingly immobilized the chest with adhesive strapping, but this provided little relief. Two weeks later, x-ray examination apparently demonstrated a collapsed left lower lobe. A lipiodol study revealed bronchiectasis of the left lower lobe. Three weeks before entry, following an episode of coughing, she raised a quart of blood, but there had been no recurrence of the massive hemoptysis.

The family and past histories were noncontributory.

Physical examination disclosed a poorly nourished, asthenic girl in no acute distress. Examination of the heart was negative. A few coarse rales were audible over the entire left lung posteriorly.

The blood pressure was 130 systolic, 90 diastolic. The temperature was 98, the pulse 90, and the respirations 20.

Examination of the urine revealed a +++ test for albumin. A review of the chest x-ray films after lipiodol instillation, taken at another hospital, showed left-lower-lobe bronchiectasis. No disease was seen in the left upper lobe and right lung.

The patient was discharged unimproved on the third day after admission.

Second admission (four months later). A left lower lobectomy was performed. The patient had a stormy postoperative course. She developed atelectasis of the left upper lobe and encapsulated empyema at the apex. Bronchoscopy revealed a great amount of mucus in the left bronchus, but no mucous plug was seen obstructing the bronchus to the upper lobe. The empyema was tapped, and very small amounts of thick material were recovered. This fluid was negative on culture.

Eight weeks after lobectomy, the left third rib was resected, and open drainage established. Multiple pockets containing air and a thin clear fluid were found over the anterior and superior surfaces of the upper lobe. After this, the temperature and pulse, which had been elevated slightly each day, gradually returned to normal. The patient was discharged four months after admission.

Third admission (one month later). One week after discharge the lobectomy incision opened at the lower end and discharged a mucoid material. The patient had a slight fever, and her physician inserted a tube in the wound for drainage. The upper empyema-drainage tube discharged a moderate amount of pus. The patient was emaciated and appeared to be chronically ill. There were three tubes in the left chest wall, two in the third intercostal space and another in the sixth intercostal space. An x-ray film of the chest revealed the tip of the upper drainage tube lying anteriorly and the lower tube posteriorly in the chest. There was still density throughout the entire left lung field except for a small collection of air at the extreme apex. The heart shadow was still markedly displaced. The patient gradually improved on open chest irrigation and left the hospital a month later.

Fourth admission (two years later). Following discharge the patient soon developed empyema on the right side, which was drained by tube at home. She spent the greater part of the next three months in an oxygen tent at home. A slow recovery was made and she was not out of bed to any extent till the following summer — about a year later. The patient then moved to a farm, where improvement was marked. Her weight rose from 65 to

98 pounds, her appetite increased, she felt stronger, and her cough lessened. She continued, however, to produce about 100 cc of foul sputum daily. She had had slight hemoptysis on only three occasions in the previous few months. Occasionally

communicating with a dilated left main bronchus. The left lower main bronchus ended abruptly, apparently at the site of the lobectomy. The mediastinum was displaced to the left but showed no respiratory shift. The right lower lung field showed



FIGURE 1 Roentgenogram Taken at the Fourth Admission Showing the Apparent Pneumothorax in the Apical Portion of the Left Pleural Cavity

she had pains in her left upper chest, accompanied by a "congested feeling," anorexia and a "dragged out sensation." Her symptoms were progressive to the time of admission.

Physical examination showed dullness, increased tactile fremitus and decreased breath sounds over the left upper lobe. Over the left lower lobe there were dullness, flatness and absent breath sounds and tactile fremitus. There were a few rales at the right base. The fingers were clubbed.

X-ray films showed that the lower half of the left lung field was completely opaque and that there apparently was a pneumothorax occupying the apical portion of the left pleural cavity (Fig 1). In the left midchest were several rounded areas of diminished density, without fluid levels, commu-

nicating with a dilated left main bronchus. The left lower main bronchus ended abruptly, apparently at the site of the lobectomy. The mediastinum was displaced to the left but showed no respiratory shift. The right lower lung field showed

increased markings with some apparent honeycombing, which had the appearance of bronchiectasis. In the lateral view this was seen to occupy the region of the middle lobe.

An operation was performed on the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR JOHN W. STRIEDER * This is a long case and demonstrates many of the vicissitudes through which a patient who has had some of the complications of major thoracic surgery goes. It is probably better to take it up in sections and to comment as we go along.

* Assistant surgeon for thoracic surgery, Boston City Hospital and Massachusetts Memorial Hospitals.

What is the significance of the attack of whooping cough? I think that is difficult to say without entering into a long discussion of the etiology of what may be the final diagnosis. The cough persisting for a year and then clearing up suggests that the patient had pulmonary disease that antedated the attack of whooping cough.

The tonsillectomy, twelve years previously, brings up the question of its relation to the subsequent course. She had no acute episode following tonsillectomy as she would have had had she developed putrid or nonputrid lung abscess as a result of the aspiration of infected secretions. The fact that the cough gradually became more severe "during the next ten years," in other words that she survived that ten years of cough, seems to me to be against acute lung abscess as a complication at that time. She raised more sputum in the morning and evening, which is usual because patients with chronic pulmonary suppuration have an opportunity during those twelve-hour intervals of puddling secretions and subsequently raising large amounts. She coughed up tenacious plugs, which may well have been fibrinous casts. It is interesting that, in patients with bronchiectasis, chronic sinusitis is a common complication that goes hand in hand with it. As Dr. Churchill has suggested, bronchiectasis is simply another infected sinus.

The question whether the atelectasis arose as a complication of the antral operation comes up. I should like to know what the anesthesia was. However, we all realize that atelectasis can be a complication of any surgical procedure under any anesthesia, whether local or general.

Hemoptysis of a quart of blood, of course, is not unusual in various types of chronic pulmonary disease, particularly bronchiectasis. Hemoptysis as a complication of bronchiectasis is commoner than hemoptysis as a complication of pulmonary tuberculosis. Since I have never seen a fatal hemoptysis in a patient who has bled as a complication of bronchiectasis, it must be very rare. It usually suffices to stimulate the patient to seek treatment, however, and in that connection it often serves a purpose.

The +++ test for albumin with the chronic pulmonary situation suggests chronic amyloidosis.

May we see the bronchograms? I do not know what Dr. Robbins will think of them, but to me, with the exception of the lateral view made earlier at another hospital, they contribute very little.

DR. LAURENCE L. ROBBINS: I think there is definite evidence of bronchiectasis in the left lower lobe.

DR. STRIEDER: These oblique views do not show it. Do you think that is something down there, below the shadow of the diaphragm on the left?

DR. ROBBINS: No; that is possibly an artefact. If it is anything of significance it is very poor filling.

DR. STRIEDER: The anteroposterior view, without lipiodol, shows atelectasis and that is all.

DR. ROBBINS: Yes. In addition to a very slight shift of the mediastinum to the left there is a dense line of increased density, which is consistent with a collapsed lower lobe.

DR. WILLIAM B. BREED: Do you mean to say that that dense line is the left lower lobe in its entirety?

DR. ROBBINS: No; but it is the sign that shows the edge of the collapsed lobe. Here is the triangular area of density that extends to the hilus, and this line is the edge of the lobe.

DR. STRIEDER: Up to this point the story is that of bronchiectasis. One thing not mentioned is bronchoscopy. To rule out the possibility of underlying foreign body, of bronchial adenoma or of other tumor, even in so young a patient, I make it a routine, in my clinic, to perform bronchoscopy on all patients with bronchiectasis. After lobectomy was done, bronchoscopy was performed, but there is no mention made of any lesion except for abundant secretions in the left main-stem bronchus. Conceivably other lesions could be overlooked because we assume the bronchoscopy was done for aspiration, and under the circumstances it is understandable that a pre-existing lesion could possibly be missed. I think it is not necessary to have a so-called "mucous plug" in the bronchus to the left upper lobe to have atelectasis of that lobe. At that time the patient had had the left lower lobe removed, and secretions in the left main bronchus would occlude the left upper bronchus so that atelectasis could occur.

We must assume that the cultures of the so-called "empyema" persisted negative over the eight-week period during which she was observed, and that drainage was undertaken perhaps with reluctance. The operative findings were also unusual for empyema, that is, if it was empyema due to pyogenic or anaerobic organisms, which might well be a complication of lobectomy. It leads one to suspect that perhaps the pathologic process was intrapulmonary rather than intrapleural and that the drainage established was actually in the lobe.

The discharge of mucoid material suggests two things: first, that the patient had opened a bronchopleural fistula and that mucoid secretions were coming from the open bronchus and, second, that she had pulmonary cyst of some sort with a communication with the pleural cavity and in turn with the incision. The mucoid drainage then became purulent, which it might well do as the result

of drainage of some weeks' standing, but there is no mention that the pus was mucopurulent in character.

Probably there was no bronchopleural fistula. This patient could tolerate open drainage with irrigation, and it seems likely that she would have had severe cough and other unpleasant symptoms if there was an open bronchus communicating with the cavity. So we are reduced to saying that either she had empyema without bronchopleural fistula, or that she had an intrapulmonary cyst without patent bronchial communications. While this preoperative film is up, I should like to ask Dr. Robbins if he attributes any significance to the suggestive annular shadow in the left apex.

DR. ROBBINS: It could be a bleb, but I cannot be positive on this film alone. I do not think it is a cavity.

DR. STRIEDER: It certainly suggests cyst, and I believe there is a pathologic process in the apex.

DR. ROBBINS: In fact there could be several small blebs in a group.

DR. STRIEDER: This was the first-admission film, and I point out the suggestion of an annular shadow in view of what is to follow.

DR. ROBBINS: For comparison this is a film taken on the last admission (Fig. 1) and shows what appear to be cavities in which there is fluid, as well as this larger one, which may be a loculated air cavity within the pleural cavity. Drainage tubes enter the chest. This is the area of resection for the lobectomy.

DR. STRIEDER: The fact that there was a large area of decreased density in the apex, anteroposteriorly, in a patient with atelectasis of the left upper lobe following left-lower lobectomy is not significant other than that this configuration is apt to denote pleural space in x-ray films. Under these circumstances I think we are justified in saying no more than that this was an intrapleural lesion.

We are therefore again thrown back on two possibilities: a residual intrapulmonary lesion, in view of the foregoing films, and an empyema without bronchopleural fistula. Despite the fact that the patient did not cough on irrigation, which is consistent with the latter, it seems to me unlikely that that was the situation.

I think we have to say there is a possibility of pulmonary cyst in the left upper lobe.

DR. ROBBINS: In this film, there is an air-filled space in the apex and there are several areas of rarefaction in the area of density in the left mid-lung field. These represent air-filled cavities. This could be air in the pleural cavity, but I think we have seen at least one case in which there was a

huge cavity in the apex that contained air, and one cannot very well tell the difference between them.

DR. STRIEDER: Can you offer any comment about this drainage tube entering into the intrapulmonary lesion?

DR. ROBBINS: Not from this film.

DR. STRIEDER: The anteroposterior view suggests to me that the lung is above the point of entrance of the drainage tube, and I think we have to take that into consideration, even though a lateral film is not available.

The problem resolves itself into a discussion of why, after left lower lobectomy for bronchiectasis, this patient continued to have symptoms of pulmonary suppuration and, as a corollary, what was the nature of these complications because of which she failed to improve. In such a complex situation the key to the solution, I think, lies largely in the x-ray films plus such other diagnostic procedures as we are able to apply, such as bronchoscopy. In this particular case, the result of bronchoscopy is not reported, but I think we can go along on supposition. If we can accept the report of the X-ray Department, based on films that are not here at the moment, there was bronchiectasis of the right middle lobe, which would account for the cough, and also intensive disease on the left side, and I think we are justified in assuming that the disability was due to the residuals in the remaining left upper lobe. The x-ray findings, the negative cultures of the material obtained on thoracentesis and the mucoid secretions strongly suggest cystic disease. Persistent atelectasis of the left upper lobe in a patient who has had left-lower-lobe lobectomy usually means obstruction of the bronchus by mucoid secretions or persistent underlying disease in the remaining lobe. That is, a patient whose remaining upper lobe stays collapsed after lower lobectomy, despite all measures to inflate it, usually has bronchiectasis or another related lesion in this lobe. On the information at hand I am unable definitely to rule out bronchial adenoma as a cause of the obstruction of the upper lobe, but I shall say that this patient probably had congenital cystic disease of the left upper lobe.

DR. TRACY B. MALLORY: Are there any questions or comments?

DR. BENJAMIN CASTLEMAN: Do you not think that, if she had congenital cystic disease of the upper lobe, the condition would have been at the first operation?

DR. STRIEDER: Not necessarily, for a variety of reasons. The upper lobe may have been completely held out by adhesions and the operator may not have thought it wise to explore farther,

knowing that the patient had disease in the left lower. Small cysts may not be palpable through surrounding normal lung tissue.

CLINICAL DIAGNOSIS

Bronchiectasis of left upper lobe.

DR. STRIEDER'S DIAGNOSIS

Congenital cystic disease, left upper lobe.

ANATOMICAL DIAGNOSIS

Cystic bronchiectasis of left upper lobe.

PATHOLOGICAL DISCUSSION

DR. MALLORY: I am sorry Dr. Churchill is not here to discuss this case since he could give us much additional information. He was able to mobilize the upper lobe readily and inspect it freely at the time he removed the lower lobe. He did not see any evidence of cystic disease and felt quite satisfied with the examination.

The major interest in this case is the anatomic finding in the upper lobe, after resection. The apex of the lung was occupied by an enormous cystic cavity. Across it ran a threadlike bridge, probably a persistent artery. In the lower part of the lung there were numerous ordinary bronchiectatic cavities, and between these cavities there was a great deal of fibrous pneumonitis and virtually no aerated pulmonary parenchyma. On the basis of the facts that at the time of the first operation it was possible to visualize the upper lobe quite well and that no suggestion of cystic disease was seen, Dr. Churchill and I believe that this must have been an acquired cyst or bronchiectatic cavity, not a congenital one, and that the period of this patient's history between the first and fourth admissions represents the time required for the development of an extreme grade of bronchiectasis. One could, of course, argue that some bronchiectasis was present at the time of the first operation, but I think it is safe to say that no massive cyst of this character could have been present. The specimen as it now appears is one that I think all pathologists who believe in congenital cystic disease would accept as such, and yet our own interpretation is the opposite. We think this was acquired bronchiectasis rather than cystic disease.

DR. STRIEDER: Would you be influenced by the fact that she did have persistent atelectasis, suggesting that she might have had previous bronchiectasis?

DR. MALLORY: It may be that the persistent atelectasis represents the cause of bronchiectasis. There is a great deal of debate on that point. I have always personally believed that persistent atelectasis is an important cause of bronchiectasis.

CASE 28522

PRESENTATION OF CASE

A sixty-two-year-old white male bundle clerk entered the hospital with the complaints of swelling of the legs and abdomen, dyspnea and frequent vomiting of three weeks' duration.

The patient dated the onset of his present illness from an accident nine months before when he slipped on a sidewalk curbing and sprained his right knee and ankle, which laid him up for five weeks. Following this period he was able to resume work and was comfortable in the daytime but was awakened several times every night by cramps in his calf. Six months previously he had developed a "dry eczema" on the dorsum of the left foot over the second and third toes. He described the lesion as a red spot the size of a five-cent piece containing many still redder spots within it. It did not hurt or itch. A change of shoes, suggested by a chiropodist, did not help, and the "eczema" slowly spread in the course of six weeks over the entire malleolus and up the internal aspect of the left calf. At that time a similar rash appeared on the dorsum of the right foot; then it in turn spread up the right leg at a rapid rate. Spots soon appeared above both knees, then on the outer aspects of both thighs, and the individual lesions began to coalesce. The lesions itched considerably but were not painful. Whitewash relieved the itching but not the spread of the lesions. During the following two months, lesions appeared in a spotty distribution over the abdomen, chest, shoulders and the flexor surfaces of the elbows and wrists. The patient observed that although these lesions in the upper part of his body were "rash-like" the ones below the knees became fiery red and blood seemed to collect beneath the skin. Vitamin B complex and haliver oil were given without improvement.

He then consulted another physician, who reported that his entire trunk and extremities were covered with a blotching erythema and an underlying fine purpura. The lower legs were studded with large perifollicular purpuric spots. There was also slight edema of the shins, and the right lower leg was distinctly swollen. A diagnosis of toxic erythema with purpura was made, and vitamin K was prescribed. The patient took 160 tablets over a period of forty days with apparent improvement; the rash disappeared from the trunk, arms and upper legs but persisted in purpuric form below both knees.

One month before entry, although the skin lesions had not changed in extent or character, the patient returned to his physician's office complaining of lower abdominal discomfort, nausea

and occasional vomiting of seven days' duration and abdominal distention of four days' duration. For seven days his legs had been swollen. His bowels had moved daily with the aid of his habitual "three quarters of an ounce" of milk of magnesia.

Physical examination at that time showed probable ascites and an icteric tint to the scleras. The hemoglobin was 14.6 gm., the red-cell count 5,000,000, and the white-cell count 6500 to 8600, with 74 per cent polymorphonuclears, 21 per cent lymphocytes, 4 per cent monocytes and 1 per cent eosinophils. The blood smear was not remarkable; the platelets were slightly decreased. The icteric index was 25, and the nonprotein nitrogen 30 mg. per 100 cc. The total protein was 6.15 gm., the albumin 3.58 gm. and the globulin 2.57 gm. per 100 cc. The bleeding time was $2\frac{1}{2}$ minutes, and the clotting time 7 minutes, with normal clot retraction. The prothrombin time was normal. The corrected sedimentation rate was 8 mm. per hour. The blood Hinton reaction was negative. The urine showed a specific gravity of 1.020, with a slight trace of albumin and a slightest possible trace of bile by the foam and iodine tests. The sediment showed rare white and red cells and unnumerable hyaline and granular casts. A gastrointestinal series showed a normal stomach and duodenum; no esophageal varices were seen.

One week prior to entry it was found that the edema of his legs had progressed upward to the thighs. He complained of much unlocalized pain in both legs, especially on the left. An abdominal paracentesis was done, but the amount of fluid withdrawn and its character were not recorded. Digitalis and Salyrgan were prescribed.

The past history included severe poliomyelitis at the age of two and a half, with temporary paralysis of the entire right side of the body, followed by gradual return of motor function. The right extremities remained slightly weak, however, and scoliosis developed. The patient had an attack of jaundice at the age of twenty. The family history was noncontributory. He denied venereal disease and the use of alcohol. He had gained 13 pounds during the preceding year.

Physical examination showed an obviously ill and uncomfortable man with jaundice of the skin and scleras. Both lower legs were covered with purpuric spots, some of which appeared to be fresh; others were fading. There was pitting edema of both legs up to the knees, but the patient stated that this had decreased considerably during the previous week, during which he had received digitalis and Salyrgan. The spine showed marked scoliosis in the upper thoracic and lower cervical regions, and the chest considerable con-

sequent deformity. The size of the heart could not be determined by percussion, and the apex impulse was neither seen nor felt. The examiner's impression, however, was that it was not enlarged. The sounds were of fair quality, and the aortic second sound was recorded as equal to the pulmonary. There were no murmurs. The rhythm was regular, at a rate 90 to 100. The neck veins were not distended. The lungs were clear. The abdomen was markedly distended, and there was shifting dullness in the flanks. Large veins could be seen in the anterior abdominal wall, but there was no hum audible at the umbilicus. A tender liver edge could be felt five fingerbreadths below the right costal margin and about the same distance below the ensiform in the midline; its upper border was percussed at the fourth interspace. The spleen could not be felt. Rectal examination showed external hemorrhoids and questionable enlargement of the left lobe of the prostate.

The blood pressure was 110 systolic, 85 diastolic. The temperature was 98.8°F., pulse 100, respirations 25.

Laboratory determinations showed a hemoglobin of 15.5 gm. and a red-cell count of 4,250,000. The white-cell count was 10,500, with 72 per cent polymorphonuclears, 18 per cent lymphocytes and 10 per cent monocytes; the smear was not remarkable. The hematocrit was 56 per cent. A single urine examination showed a specific gravity of 1.003 and gave a + test for albumin; there was no sugar or bile. The sediment showed 3 red cells and rare white and epithelial cells per high-power field. A stool was tan colored and contained bile; the guaiac test was negative. The serum nonprotein nitrogen was 82 mg. per 100 cc., and the prothrombin time 41 seconds (normal, 22 seconds). The liver function test showed 95 per cent retention of the dye in the serum. The serum protein was 7.8 gm., the albumin 4.5 gm., and the globulin 3.3 gm. per 100 cc. An electrocardiogram was interpreted as follows: normal rhythm, rate 85; low voltage of the QRS complexes; low T waves, slightly diphasic in Leads 1 and 2, having the appearance of digitalis effect; no abnormal axis deviation; P waves and PR intervals normal; normal R₄ and a rather low T₄.

During the six days in the hospital his many discomforts rapidly increased and his strength diminished. Chloral hydrate, Nembutal and Empirin Compound failed to give relief. A single dose of 1/6 gr. of morphine made him drowsy for twenty-four hours. Two abdominal paracenteses yielded less than a liter of fluid each. The specific gravity was 1.009. It contained 160 white cells (110 polymorphonuclears, 30 lymphocytes and 20 mono-

cytes) and 880 red cells per cubic millimeter. The sediment was negative for tumor cells.

On the sixth hospital night the house officer was called at 3:30 a.m. He found the patient dead, with large amounts of dark-red blood still oozing from the nose and mouth.

DIFFERENTIAL DIAGNOSIS

DR. ALFRED KRANES: It seems unlikely that the fall occurring nine months before death had much to do with this patient's illness, and I shall dismiss it from consideration, except to say that five weeks is a little long to be incapacitated from work because of a sprained knee and ankle. It raises the question whether some serious underlying disease was not already present, to which attention was directed by the fall. The appearance of the rash shortly thereafter is probably coincidental. Why a purpuric rash should itch puzzles me, for it has always been my impression that pruritus does not occur with purpura. Since clinical jaundice was noticed shortly thereafter, a possible explanation for the itching may have been the jaundice, rather than the rash to which it was attributed.

I regret that so little information is given concerning the first physical examination, which mentions only "probable ascites and an icteric tint to the scleras." Presumably the purpuric rash was present at that time. What would interest me more is a statement about the liver and spleen, since the former was easily felt on subsequent examination, and it would be important to know whether the apparent rapid increase in size was actually true. Since it is not mentioned, I am going to assume that the liver was not felt initially, and that it did rapidly increase in size, becoming tender in the process. The laboratory data, except for the slight rise in the icteric index, are normal at this examination.

The past history is of interest because of the attack of jaundice at twenty. Presumably this was catarrhal jaundice, which is the commonest type at this age and which may be related to his terminal illness, obviously involving the liver. Most cases of catarrhal jaundice clear up, leaving no residual liver damage, but a small percentage may either develop subacute yellow atrophy or show evidence of cirrhosis years later.

The problem is a very interesting one, and I am not at all sure that I can adequately explain it. The opening sentence of the history immediately suggests the possibility of some sort of heart disease, for which he was apparently treated with Salyrgan and digitalis. Furthermore it is implied that this resulted in lessening of the edema of his legs. Certainly the presence of an enlarged ten-

der liver, ascites and edema of the legs is consistent with cardiac failure. However, I can find little in this story to support such a diagnosis. Although dyspnea is stated as one of his chief complaints, there is no further mention of it anywhere in the history. Furthermore there was no clinical evidence of pulmonary congestion, or of increased venous pressure except in the abdomen. If the large tender liver was due to cardiac failure, the neck veins should also have been distended. Nor did the examination of the heart itself show any evidence of disease, although the absence of enlargement clinically is not too reliable. The patient was probably too ill for x-ray examination. As for the electrocardiogram, all it reveals to me is a digitalis effect and the type of tracing one might expect in any debilitated patient without heart disease. I should like to ask Dr. Bland for his interpretation.

DR. EDWARD F. BLAND: We thought that there was no evidence of intrinsic disease of the cardiovascular system. The electrocardiogram was taken because of interest in the possible presence of heart disease secondary to the thoracic deformity.

DR. KRANES: I think we can therefore safely dismiss heart disease from consideration. The past history, the presence of jaundice and ascites, evidence of collateral circulation in the abdominal wall, an easily palpable liver, the terminal hematemesis and the clinical effect of a small dose of morphine — all these factors are strong evidence in favor of some sort of intrinsic liver disease, probably cirrhosis, which I am inclined to believe was present. What type of cirrhosis is difficult to say without more history, but I favor a toxic cirrhosis despite the absence of known toxic factors. It would be of some interest to know whether he took any drugs such as cinchophen for relief of the pains in his legs following his fall, or whether he received injections of gold salts for what may have been diagnosed as an arthritis. Presumably not. There is no evidence that any arsenical drugs had been administered. The question of drug idiosyncrasy must be further emphasized because of the presence of the purpuric rash, which we have not explained, and to which I shall return in a moment. Despite the evidence in favor of cirrhosis there are a number of disturbing factors that argue against it.

In the first place his illness progressed much more rapidly than the usual case of cirrhosis, in the absence of any signs of subacute yellow atrophy. Furthermore, I cannot understand why the liver should have increased so rapidly in size, if that observation was correct. To be sure, estimates of liver size are likely to be quite erroneous, but this

was a comparative observation made at different times and is therefore likely to be somewhat more reliable. Then too, cirrhotic livers are not likely to be as tender as this one was. A tender liver is usually a congested one, or one that contains a malignant tumor. Also, the absence of splenomegaly is disturbing in a patient who has cirrhosis. Finally, I cannot see how a diagnosis of cirrhosis of the liver explains the most prominent clinical feature of his illness—the purpura. And I might add that I can find no other satisfactory explanation for it. A bleeding tendency does occur in severe liver disease with an increased prothrombin time; but I have never heard of its being confined so exclusively and so extensively to the skin, as in this case. The skin manifestations of a prolonged prothrombin time are likely to be diffusely ecchymotic rather than discretely purpuric. The fact that the purpura preceded by months the clinical evidence of liver disease need not disturb us, for I have seen patients admitted to the Emergency Ward with repeated epistaxes, only to turn up a year later with obvious cirrhosis. However, I find it difficult to believe that the purpura in this patient was in any way related to his liver disease.

I do not know what was the cause of the skin lesions. There is no evidence whatsoever pointing toward the usual causes of purpura, such as a primary blood dyscrasia and drug ingestion. The possibility of scurvy occurred to me in view of the perifollicular hemorrhages and the pains in the legs. Although he was extensively treated with vitamins A, B, D and K, there is no mention of his having received any vitamin C. Scurvy is an unusual disease these days, but even so it seems improbable that it was missed. Might I ask about his dietary history?

DR. BLAND: The patient had been on an adequate diet.

DR. KRANES: That, I think, adequately disposes of the question of scurvy. Since I can find no satisfactory explanation for it, I shall have to call it purpura of undetermined etiology.

For the reasons that have already been stated, cirrhosis does not completely explain this picture, and it becomes necessary to consider whether any additional factors were present. The facts that the disease progressed fairly rapidly and that the liver increased in size while becoming tender immediately raise the question of cancer. If this patient had malignant disease I can see no way of making the diagnosis without further study, which was precluded because of his condition. Metastatic carcinoma could explain much of it, but without any anemia or obvious primary focus it remains

only a possibility. Lymphoma of the liver is not only quite uncommon without other evidences of the disease, but a fever usually accompanies it, which was not present in this case. Another possibility is hepatoma, for which we seem to have the proper background—a pre-existing cirrhosis. Again one can only mention the possibility.

A rare possibility, which might be mentioned in an attempt to explain the rash, is acute disseminated lupus erythematosus, the skin lesions of which may be purpuric. It would explain the rash, the joint and abdominal pains, the ascites and the terminal renal failure without hypertension. However, it rarely occurs in men and, so far as I know, never involves the liver. We can therefore dismiss it. I do not believe there was any primary renal disease, despite the urinary findings and nitrogen retention. These can be attributed to the fact that there was terminal renal failure in an otherwise very ill patient.

In conclusion, my belief is that this patient had cirrhosis of the liver, but since this does not adequately explain the whole picture, I raise the question whether or not something else was present, such as a hepatoma.

DR. EUGENE R. SULLIVAN: Dr. Bland, you saw this case: would you care to add to the discussion?

DR. BLAND: It was extremely difficult to get an adequate history from this patient. In spite of the marked thoracic deformity of long standing we were convinced that the heart action was entirely competent. We agreed that cirrhosis of the liver was most likely; but the rather rapid progression in the size of the organ, its tenderness and the high degree of abdominal venous stasis developing in the course of a month suggested to us, as it has to Dr. Kranes, some additional complication, such as cancer.

I think it is important to emphasize the profound narcosis that a small dose of morphine produced in this patient. This in turn lent additional support to the diagnosis of extensive hepatic disease.

DR. S. PETER SARRIS: Should not hepatic-vein thrombosis be considered? That would explain the enlargement of the liver, apparently increasing under observation, and the fact that the patient failed more quickly than most of those with cirrhosis.

DR. KRANES: In thinking over this problem I had considered that, but because of its rarity did not mention it. However, it is distinctly possible and would explain some of the atypical features.

CLINICAL DIAGNOSES

Cirrhosis of liver.
 Subacute hepatitis.
 Abdominal cancer?
 Terminal hemorrhage, from esophageal or possibly gastric varices.

DR. KRANES'S DIAGNOSES

Cirrhosis of liver.
 Hepatoma?
 Purpura (? cause).

ANATOMICAL DIAGNOSES

Primary liver-cell carcinoma (hepatoma), with extension into and obstruction of inferior vena cava.
 Cirrhosis of liver, toxic.
 Ascites.
 Icterus, slight.
 Gastric erosions, multiple, small, mucosal.
 Duodenal ulcer.
 Arteriosclerosis, moderate: aortic, coronary and peripheral.
 Pulmonary tuberculosis, healed, localized: apical.
 Kyphosis: thoracic.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: I happened to prepare the clinical abstract of this case personally and, as I did so, amused myself by attempting to guess how it would be discussed. I expected that the discussor would briefly consider and quickly eliminate kyphoscoliotic heart disease. I then expected him to take up the confusing data regarding liver insufficiency—on the one hand, the low prothrombin value, the bromsulfalein retention and the terminal gastric hemorrhage, and on the other hand, the absence of demonstrable esophageal varices, of splenomegaly, of leukopenia, of lowering of the serum protein or of reversal of the albumin globulin ratio. I expected that he would reach the conclusion that cirrhosis of the liver alone could not explain the picture, and that he would advocate either malignant tumor or mechanical obstruction of the vena cava as the underlying factor. Dr. Kranes has reached the correct diagnosis by a slightly different route.

I should like to read two clinical notes from the hospital record, written before the patient died. The first is by Dr. Bland:

My first impression is that the chief difficulties are portal obstruction and hepatic insufficiency of rather acute onset and probably complicating chronic asymp-

tomatic liver disease. The normal serum protein and prothrombin determinations are disturbing.

The thoracic deformity is a further handicap and has probably resulted in some strain on the right heart, but I am doubtful that cor pulmonale or inflow stasis to the heart is the important feature behind the jaundice, dermatitis, large liver, ascites and dilated veins below the diaphragm.

I cannot feel the spleen; I hear no umbilical hum, and the heart on physical examination does not seem to be enlarged. The pulmonic second sound is not suspiciously loud, and there is no gallop. I cannot be certain of the cervical veins, but those on the dorsum of the hand seem slightly swollen above the level of the heart (? secondary to abdominal tension).

Dr. Chester M. Jones saw the patient in consultation and commented as follows:

I cannot make a diagnosis. There is obvious embarrassment of the venous return through the vena cava. It is not possible to connect adequately the edema and the ascites with hepatic failure. If the ascites is purely mechanical and due only to intrahepatic disease, the absence of anemia, varices, splenomegaly and lowered serum albumin are unusual. I think that caval pressure must be considered and that carcinoma must be ruled out. Regardless of the underlying diagnosis, everything is exaggerated by his deformity. I believe he has an incurable disease and advise peritoneoscopy as the best means of establishing a diagnosis.

On post-mortem examination, we found a cirrhotic liver with a large nodule of hepatoma in the right lobe. This had spread, as it so often does, in the form of a tumor thrombus infiltrating along the hepatic venous radicles. A thrombus of tumor protruded from the main hepatic vein and was continuous with a similar mass that almost completely obstructed the inferior vena cava for its upper 7 or 8 cm. It stopped just short of the mouth of the cava at its junction with the right auricle. The cirrhosis was an old inactive one of the toxic type. The spleen was not enlarged, weighing only 170 gm., and there were no esophageal varices. The final hematemeses, which caused death, probably resulted in part from an extremely severe erosive gastritis with some fifty small, shallow, hemorrhagic erosions, mostly along the greater curvature, and in part from an acute duodenal ulcer about 2 cm. in diameter.

The heart was slightly enlarged but showed no evidence of cor pulmonale. The kidneys were large but showed only severe passive congestion, undoubtedly secondary to the caval obstruction. There was healed apical pulmonary tuberculosis, and one very large, densely calcified bronchial lymph node was found. There was nothing to explain the skin lesions, unless it was the liver disease.

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PASS THE AMMUNITION

We are reminded every so often that where there is no vision the people perish. Our vision has occasionally become very dim even if it has never entirely faded, and this has usually occurred when the present has seemed most fruitful and the future most promising. It is only when we are combating adversity that we realize the sweetness of its uses, and then, for a time, the veil is lifted from our eyes.

A year ago at Christmas time we had embarked on a common enterprise, each of us sharing the hopes of victory and risking the dangers of defeat. We were confused and uncertain then, fearful of our weaknesses and ignorant of our strength. We knew what we had been spared

of the miseries of other peoples, but we did not know how long we might be spared them, or what else the future might contain. We knew only that a year of giving ground was in store for us—a year of sparring for time before we had strength to strike back.

Some of our weaknesses have been uncovered, and we know now that we have strength and courage and initiative in spite of the soft years that are behind us. We have put a girdle around the earth, if not, like Puck, in forty minutes; our youths are standing to their arms by Greenland's icy mountains and on Africa's golden sands. They are, to borrow further from the same literary source, basing their activities on the coral strands of India; and the heathen who, in his blindness has bowed down to wood and stone, bows also before the fire of our guns of destiny.

We are celebrating at this season the great pageant of Christianity, but it is as militant Christians that we are observing it. As we go forth to war, the Son of God goes with us. This year we will praise the Lord, as usual, but we will also pass the ammunition.

POLIOMYELITIS RESEARCH

DURING the last few years, much has been added to our scant understanding of an age-old disease, poliomyelitis. The virus, for example, has been isolated from the stools of patients and contacts and has been found both in sewage and in flies collected in epidemic areas. It is now thought, moreover, that the common portal of entry in man may be the alimentary tract, as well as, or perhaps in place of, the long-recognized route through the olfactory mucous membrane. A study of the transmission of the virus along axons and an evaluation of the various factors affecting its progress to the central nervous system are being actively prosecuted. The whole subject of neurotropic viruses and of their action on the body is, indeed, in the forefront of medical research today.

Not the least significant in this advance is the

work of Howe and Bodian.* They have shown that the virus of poliomyelitis is highly specific for the neuron and, in the peripheral nerves, migrates along the axons themselves rather than within the sheaths of the nerves. The rate of progress, according to their estimate, is 2 or 3 mm. per hour. Moreover, if the direct axonal pathway is not open, the virus may progress centrally through distant autonomic ganglions. How the virus penetrates the epithelium is still obscure, as is the problem why some intestinal contents tolerate the virus and some do not. In a rhesus (monkey), for example, the intestinal secretions are unfavorable for effective survival of the virus, whereas in a chimpanzee and in a cynomolgus (monkey), it is regularly found in the stools. These and other problems of host susceptibility are still matters for future research.

A most striking finding is their demonstration that susceptible nerve cells may become refractory during the time their injured axons are being reconstituted. The nature of this reaction is unknown, but it may depend on the chemical constitution of the cell protoplasm. The cells showing refractoriness to poliomyelitis still appear to be alive and capable of carrying on their normal functions. Such findings may well lead to changes in the treatment of the disease in human beings.

Other investigations by Howe and Bodian deal with the humoral mechanisms tending to protect the host at the portal of entry of the virus, the variability of susceptibility in different parts of the central nervous system, the local immunity of any one part afforded by a previous attack and the general problem of the control of poliomyelitis. On the last point, the following is quoted from the final paragraph of their summary:

At the present time the control of poliomyelitis can be attempted along three lines, namely, preventing the virus from reaching the susceptible individual or, failing this, arresting the progress of the virus before it has reached the central nervous system or, lastly, limiting the spread of virus within the central nervous system. The development of these approaches is proceeding in a somewhat more satisfactory fashion with

the acquisition of newer knowledge concerning the dissemination of virus, the portals of entry, and the forces which make for resistance in the organism. It seems not unlikely that the next few years will see more practical fruition of these efforts.

OBITUARY

FRANCIS SEDGWICK WATSON†

1853-1942

It is the difficult duty of the writer of such a notice as this to try to give a word picture of a remarkably brilliant, handsome and versatile man, a character unique in the writer's experience, and most lovable. He was an excellent surgeon, a remarkable linguist, a most loyal friend, a faithful servant of the Boston City Hospital and the Harvard Medical School, a man of high ideals and fine sensibility. He was vibrant with the joy of life, and a most entertaining companion, a thorough sportsman and lover of the outdoors. Of his many summers spent on the Saguenay, he has left a most delightful account in that rare book, *A Bundle of Memories*, which it has been my privilege to read. In whatever he undertook, his ideals were of the highest. As one of his juniors on the staff of the Boston City Hospital I can give personal testimony to his kindness and helpfulness to the younger and less experienced members of the staff, to his readiness in encouragement and his frankness in criticism.

He was born in Milton, Massachusetts, on May 31, 1853, the son of Robert Sedgwick and Mary Hathaway Watson. He graduated from Harvard College in 1875, and from the Harvard Medical School in 1879. He was surgical intern at the Massachusetts General Hospital in 1878, his colleague being Dr. John B. Wheeler, that sterling surgeon of Burlington, Vermont, with whom he maintained a delightful and intimate friendship the whole of his long life. Their deaths came within a few months of each other.

The leading surgeons of the hospital at that time were Dr. Henry J. Bigelow, Dr. Richard M. Hodges, and Dr. C. B. Porter, all of whom he greatly admired, and of whom he has written delightfully in his *Bundle of Memories*. He had the greatest admiration for Dr. Bigelow, and being like him, a tall, handsome and brilliant man, with a very marked personality, he reminded his associates of that famous surgeon in his manner and ways of speaking, especially before the students. His real instinct for showmanship helped him to

*Howe, H. A., and Bodian, D. *Neural Mechanisms in Poliomyelitis*. 234 pp. New York: The Commonwealth Fund, 1942.

†Read at the annual meeting of the Boston Surgical Society, Boston, December 7, 1942.

emphasize the points of his lectures and clinics, and his brilliant wit made them most entertaining.

After leaving the hospital, he studied in Europe for two years. Of these years he writes, "Those were glorious years, those years we passed in Europe, putting the finishing touches to our medical education, and while yet free from serious care and responsibilities." He studied at Vienna, after two months spent in a German family in Dresden in order to learn the language, and in Strasbourg he worked in the laboratories of Waldeyer and von Recklinghausen. On his vacations, he traveled extensively in Italy, Spain, France and North Africa: His description of his travels reveals a keen appreciation of the art, architecture, music and life in these countries as seen by a young, enthusiastic and brilliant observer. I do not know of any writing on travel more interesting and amusing than this part of his *Bundle of Memories*.

On his return to this country, he started practice in Boston, beginning by doing a dispensary district. He was surgeon for genitourinary diseases at the Boston Dispensary, and surgeon to out-patients at the Children's, Boston City and Carney hospitals. He was instructor and lecturer on minor surgery and genitourinary diseases at the Harvard Medical School. In 1894, he became visiting surgeon at the Boston City Hospital, and in 1896 was the head of the Genitourinary Department at Harvard, and was president of the American Society of Genito-Urinary Surgeons, presiding at the triennial meeting in Washington. In 1890, he had been a delegate from the American Association of Andrology to the International Medical Association in Berlin. In 1897, he was invited by the Russian Committee of the International Medical Congress, which met in Moscow, to be one of the honorary presidents of the Congress of the Society of Surgery. He attended the meeting, and astonished and delighted the natives by giving his address in Russian, which, needless to say, was a result of much study and a *tour de force* of memory. Of this he writes:

The president called on me to speak and I began in French, saying that I would very much like to respond to our hosts in their own language, and that if they would be indulgent, I would make the attempt to do so. Then I sailed in. With the first words a low murmur arose from the Russians. I at once felt that I had placed the accent on the wrong syllable somewhere in the phrase, and broke into a cold perspiration as the vision of the long journey to Siberia, which was called into being by my heated imagination, arose before me. I felt persuaded that I must have said "to hell with the Tsar," or some equally damning words, and braced myself to meet the worst. Then I noticed that the Russians were advancing toward me,

holding their champagne glasses in their hands, and smiling encouragement. Being thus relieved as to my fate, I went on with the following few words.

These few words proved to be a delightful message of thanks to the Russians for their warm hospitality, and a statement of the pleasant memories he should carry home, and wishes for their good fortune, happiness and success. The enthusiasm of the Russians for his address passed all bounds, and, therefore, many healths were drunk, and he had to pretend to drink them in order to avoid direful consequences.

In 1908 with Dr. John H. Cunningham, Jr., he published a complete textbook on diseases of the genitourinary system, which has remained a standard treatise to this day.

Besides the local and national societies, he was a member of the International Surgical Society, the Urological Society of Germany and that of Russia, a corresponding member of the Surgical Society of Moscow and an active member of L'Association Française d'Urologie (vice-president in 1911). In 1921 he was elected honorary president of Société Internationale d'Urologie.

In 1906, he resigned as surgeon-in-chief at the Boston City Hospital and lecturer at the Harvard Medical School after twenty-five and thirty years, respectively, of service. He was a charter member of the Tavern Club, and contributed a brilliant play which he wrote and staged among many other contributions to its proceedings.

He was married at Boston, June 16, 1886, to Mary Perkins, who died at Boston, September 19, 1917. In October, 1918, he married Genevieve Walker. He had one daughter, who died in infancy, by his first marriage.

In his surgery, he was forward-looking and courageous. He lived through the time when prostatectomy became a recognized operation, and did much, by example and writing, to help on the adoption of this operation, which has been so great a boon to many sufferers.

In 1888, Dr. Watson presented in monograph, the first classification of the gross pathology of the prostate and formulated the proper surgical procedures to deal with the various types. He emphasized the advantage of attack of certain intravesical growths suprapubically and smaller hypertrophies, both sclerotic and malignant, through the perineum. These principles remain the same today, and it is generally recognized that it was his foresight that outlined the surgical principles now employed.

He was also a pioneer in the electrical destruction of tumors of the bladder, for which he invented an instrument to be employed through suprapubic exposure, as well as the destruction of prostatic hypertrophy with a galvanocautery instrument of his own invention, which was employed by intraurethral manipulation, a procedure that antedated those of Friedenburt and Bottini.

In the New England Surgical Society, who of the members can forget his brilliant addresses at two meetings, in Portland, Maine, and St. Albans, Vermont, where his wit flashed like a comet across the level of our scientific monotony? The dinner at Vermont was held on one of the Lake Champlain steamers, and the combination of the good dinner, the lovely lake and Frank Watson's address cannot soon be forgotten.

I cannot close this notice of a beloved, loyal and brilliant friend without saying a word about his admiration and appreciation of his older friends and colleagues, such as Drs. David Cheever, Ned Bradford and George W. Gay, of whom he wrote most charmingly in his *Memories*. Loyalty and kindness were his chief characteristics, and there was not a mean, jealous or unkind drop of blood in his body. He differed from most of us in his facility and clearness in the expression of his thoughts and feelings, and these thoughts and feelings to the last were those of a good friend and gallant gentleman.

F. B. L.

MEDICAL EPONYM

SKODAIC TYMPANY

This is described by Dr. Joseph Skoda (1805-1881), chief physician of the Vienna General Hospital, in his book, *Abhandlung über Perkussion und Auskultation* [*Treatise on Percussion and Auscultation*] (Vienna, 1839). A portion of the translation from the third edition (Vienna, 1844) follows:

It would seem contrary to the laws of physics that a lung containing a small amount of air should give a tympanic note, whereas the same lung with an increased air content is not tympanic. The fact, however, is well established and is borne out not only by experiments made on the cadaver, which will be referred to later, but by the constant finding that in the presence of exudate in the thoracic cavity, which entirely compresses the lower part of the lung and markedly reduces the volume of the upper lobe, the percussion note is distinctly tympanic over the upper part of the thorax.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECRETARY'S OFFICE

Dr. Frank H. Lahey, chairman of the Directing Board of the Procurement and Assignment Service, has requested the publication of the following statement, dated December 16.

MICHAEL A. TIGHE, *Secretary*

* * *

It is of the utmost importance that the Procurement and Assignment Service for Physicians, Dentists and Veterinarians, immediately has the name of any doctor who really is willing to be dislocated for service, either in industry or in overpopulated areas, and who has not been declared essential to his present locality. This is necessary if the medical profession is to be able to meet these needs adequately and promptly. We urgently request that any physician over the age of forty-five who wishes to participate in the war effort send in his name to the state chairman for the Procurement and Assignment Service in his state.

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

TOXEMIA AND ECLAMPSIA (*Concluded*)

Of the remaining 19 cases of toxemia and eclampsia, 6 patients died undelivered and 13 were delivered normally or by vaginal operation.

The first of the 6 undelivered patients was a woman in her second pregnancy on whom a diagnosis of essential hypertension had been made before pregnancy, since her systolic blood pressure consistently ranged from 160 to 180. Following an attack of abdominal pain the blood pressure rose to 290 systolic, 140 diastolic and she was sent immediately to the hospital. After a convulsion she went into coma and died undelivered. Autopsy revealed scattered hemorrhages throughout the viscera, cerebral hemorrhage and acute peripheral necrosis of the liver. This patient should not have been allowed to become pregnant.

The second patient, a multipara who had had no prenatal care, was known to have chronic hypertension. She was not seen until the seventh month, at which time she had a convulsion. She was immediately hospitalized, being comatose on arrival, and died undelivered. It is probable that

this patient should not have been allowed to become pregnant; however, intelligent prenatal care might have averted this disaster. Cerebral hemorrhage was probably the immediate cause of death.

The third case was that of a patient who had not seen a physician throughout her pregnancy, was seized with convulsions when at term and was hospitalized. She was unconscious on entry; the blood pressure was 186 systolic, 114 diastolic, there was albumin in the urine, and the fetal heart was inaudible. The patient died undelivered. Fortunately an autopsy was performed, which revealed eclampsia and acute passive congestion of the kidneys. This was probably an unnecessary death. It is shocking that no medical advice was sought or given during pregnancy until eclampsia itself was present.

The fourth patient, a primipara who had had no prenatal care, was admitted to the hospital in active convulsions, which were followed by coma. Conservative treatment alone was employed; death occurred twenty-four hours after admission. The patient was undelivered, but a stillborn fetus was obtained by post-mortem cesarean section. Autopsy showed focal necrosis of the liver, fatty degeneration of the heart and cardiac dilatation. There is little to be said about this case. Present-day knowledge would lead one to suppose that intelligent and adequate prenatal care would have averted this catastrophe. Certainly eclamptic symptoms existed a few weeks before the convulsions occurred and, if recognized, might have responded to treatment directed toward the removal of the fetus before the eclamptic seizures occurred.

The fifth patient was a primipara who had a normal pregnancy until she reached the twenty-second week, at which time she was "taken ill" while at the beach and advised to return to her own home. Shortly after reaching home she had a convulsion and was seen by her physician, who found a blood pressure of 200 systolic, 140 diastolic, considerable edema and a large trace of albumin in the urine. She was immediately sent to the hospital, where labor started spontaneously the day after entry, but went steadily downhill and died undelivered. This was a very early case of eclampsia. It is possible, although the history does not suggest it, that some chronic kidney involvement was behind this. No attempt to operate was made, and from this standpoint the treatment can in no way be criticized.

The history of the sixth patient is inadequate. At eight and a half months she apparently developed acute eclampsia, and the baby was not delivered. Autopsy revealed fulminating toxemia and central necrosis of the liver.

The 13 remaining patients were delivered normally or by vaginal operation. The first patient was a twenty-three-year-old primipara who had had a nephrectomy several years previously and who, at eight and a half months, had a blood pressure of 160 systolic, 100 diastolic, and a large trace of albumin in the urine. She was hospitalized, and an attempt at induction of labor by packing the cervix was unsuccessful. The vagina, however, was packed with gauze the following day, and labor was initiated. The next day she had a convulsion, at which time she was said to be fully dilated. Delivery was accomplished by forceps, but the patient continued to have convulsions and died thirty-six hours post partum. It is possible that delivery should have been considered sooner; furthermore, the practice of packing of the cervix to induce labor is antiquated. The existence of only one kidney was undoubtedly contributory to the toxemia that resulted fatally.

The second patient, whose first baby had been delivered by cesarean section, had had inadequate prenatal care. On the twenty-first week she was presumably all right, but on her next visit, five weeks later, she had an increased blood pressure with albuminuria and edema. She was immediately hospitalized, but conservative treatment did not achieve any benefit. The patient went into convulsions; labor, which was normal, was induced by rupture of the membranes and was followed by delivery of a macerated fetus. The patient did not regain consciousness and died shortly after delivery. The treatment in this case cannot be criticized. The patient herself was at least partly to blame for not making regular prenatal visits.

The third patient, a thirty-six-year-old primipara on whom a diagnosis of essential hypertension had previously been made, did not consult her physician until approximately six months pregnant, at which time she had a systolic blood pressure of 260, a urine filled with casts and a +++ test for albumin. Instead of being immediately hospitalized, she was sent home to bed. Two weeks later she was sent to the hospital. Labor began spontaneously the day after entry, and she delivered herself of a macerated fetus. She apparently had a convulsion during delivery, which resulted in a cerebral hemorrhage; she did not recover consciousness and died a few hours later. It is questionable whether this patient should have ever been allowed to become pregnant, and in the event of pregnancy, abortion should have been advised at her first prenatal visit. She should have been hospitalized when first seen; and an early delivery when the symptoms did not abate might have prevented this fatality.

The fourth patient was a woman in her second pregnancy who was given adequate prenatal care from the beginning of pregnancy; she was classified as having a Grade I pre-eclampsia. Before delivery the blood pressure was 160 systolic, 98 diastolic. She went to term and was delivered normally, convalescence being uneventful until the thirteenth post-partum day, when she had convulsions, which were followed by a cerebral hemorrhage. Death occurred three days later, and autopsy revealed cerebral thrombosis and hemorrhage and chronic rheumatic heart disease; there was no reference to pathologic lesions of the kidneys. In no way can the handling of this case be criticized.

The fifth patient was a primipara who, at eight and a half months, had definite toxemia associated with separation of the placenta. A normal delivery was followed by two convulsions two days afterward, from which the patient did not recover. There was absolute suppression of urine post partum. The treatment of anuria associated with toxic separation of the placenta by decapsulation of the kidney has often proved successful, and its use might have done some good in this case.

The sixth patient was a multipara who was seen only once during her pregnancy, when just short of seven months. Ten days afterward she had a cold, with a temperature of 104°F. Labor started spontaneously the following day, and a premature infant was delivered. That evening the patient became desperately ill and was sent to the hospital, where she died shortly after entry. Autopsy revealed toxemia of pregnancy. This history is so sketchy that it is difficult to make the information given to the investigator correlate with the facts. The autopsy, however, showed that toxemia was the real cause of this fatality, although the attending physician made no mention of increased blood pressure or albuminuria. This patient had neither adequate prenatal care nor intelligent care after she had seen her physician.

The seventh patient, a primipara who was said to have a large trace of albumin and a systolic blood pressure of 140 at five months, was not seen again for two weeks, at which time the physician was summoned to her home and found her complaining of headache and blindness, with a systolic blood pressure of 200 and a urine solid with albumin. The following day she delivered herself spontaneously of a stillborn infant. Acute anuria developed, and death occurred six days afterward. This patient was not given intelligent or hardly humane treatment.

The eighth case was that of a primipara who was known to have had hypertension and albuminuria and who had had excellent prenatal care. The only criticism of the case is that the patient

was allowed to go into spontaneous labor at term with a systolic blood pressure of 200 and without being hospitalized before delivery. Convulsive seizures occurred after delivery, and the patient died of anuria fifteen days post partum. This is a case of post-partum eclampsia that undoubtedly was the result of hypertensive kidneys. Had this patient been delivered at eight months, when the baby was viable, the fatality in all probability would not have occurred.

The ninth case was that of a patient who had been toxic during pregnancy two years previously and had been delivered of a stillborn infant. She was not seen until the seventh month of her second pregnancy, at which time she was said to have been normal. When near term she became irrational and the systolic blood pressure rose to 160, with marked edema and moderate albuminuria. The toxemia was accompanied by jaundice. Six hours after the induction of labor by artificial rupture of the membranes a stillborn fetus was delivered, and the patient expired shortly after delivery from circulatory collapse, which may well have been due to the toxic myocarditis that is occasionally associated with severe toxemia. The jaundice suggests liver involvement. This patient was not given adequate prenatal care, especially in view of her previous toxemia.

The tenth patient, a primipara who had had no prenatal care, gave an entirely negative history up to the time of labor, which started prematurely at six and a half months; she was sent to the hospital, and delivery was accomplished soon after entry. A convulsion occurred immediately after delivery, and anuria was followed by death one week later. Intelligent prenatal care would have undoubtedly averted this disaster.

The eleventh patient was a primipara who had had moderately intelligent prenatal care and was said to have been normal until the end of the seventh month, when the blood pressure was 160 systolic, 100 diastolic. One week later the blood pressure returned to normal, but three weeks before the onset of labor it again became elevated. The patient was not seen again until she had a convulsion, at which time the blood pressure was 190 systolic, 120 diastolic. A stillborn child was delivered not long after hospital entry. Anuria developed immediately after delivery. Probably a cerebral hemorrhage was the immediate cause of death, which occurred twelve hours after delivery. Of course, this patient should have been seen more frequently at the end of pregnancy. It is difficult to understand how any physician could let three weeks go by without seeing a patient whose systolic blood pressure was 190.

The twelfth patient, a primipara who had had adequate prenatal care, was sent to the hospital at the beginning of the tenth month because of a systolic blood pressure elevated to 180, edema and considerable albuminuria. The day after entry she had two convulsions; labor started spontaneously, and a stillborn infant was delivered by low forceps. The patient was comatose after delivery and died twelve hours later. Autopsy was performed, but unfortunately the report could not be found. In this case, delivery should have been considered earlier.

The history of the thirteenth and final case is inadequate; apparently toxemia proved fatal in a patient who was delivered normally at term.

In the entire series of 27 cases, six autopsies were performed.

In reviewing these cases of toxemia and eclampsia, it is extremely gratifying to find that in none was *accouchement forcé* resorted to. In only one case can the operative management be criticized, this being the one in which cervical packing was attempted. It is deplorable that so many of these cases were treated by cesarean section after eclampsia had established itself, since it is almost an axiom that an eclamptic seizure contraindicates section. It is also deplorable that some of these patients with eclampsia had no prenatal care, and one cannot help but believe that some of them at least might have been saved had they been seen routinely during pregnancy. The number of patients who died undelivered is noteworthy. Eclampsia may certainly be a rapidly fatal disease.

The two patients on whom nephrectomy had been performed years previously illustrate the potential seriousness of pregnancy in a patient with one kidney. Such patients should be watched more carefully than the normal pregnant woman, and it might be well, for the purpose of saving added work on the one remaining kidney, to anticipate labor by the proper method of emptying the uterus after viability.

The tabulation for 1941 shows an increase of 2 in the deaths from toxemia and eclampsia as compared with that for 1940. An analysis of these deaths in 1941 clearly shows that many of them were preventable.

A CORRECTION

I wish to correct a statement made in the report to the Council of the Massachusetts Medical Society of my survey of the state-aided cancer clinics, which appeared in the November 12 issue of the *Journal*.

When I visited the clinic at the Boston Dispensary I was told they did not have facilities for treatment with a high-voltage x-ray machine. Mr. Frank E. Wing, the director, now tells me I was misinformed and that a 200,000-volt machine for patients requiring that form of treatment was installed several years ago.

CHANNING C. SIMMONS, M.D.

DEATHS

BRIGGS—CHARLES A. BRIGGS, M.D., of Assonet, died December 14. He was in his eightieth year.

Dr. Briggs received his degree from the Long Island College of Medicine in 1889. He was appointed school physician soon after he went to Assonet to practice. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and a daughter survive him.

DIXON—ROBERT B. DIXON, M.D., of Boston, died December 16. He was in his eighty-seventh year.

Born in Damariscotta, Maine, he received his degree from Harvard Medical School in 1879. For twelve years he was physician at the Boston Dispensary and was commissioner on the Massachusetts Nautical Training School. He had been a director of the Robert B. Brigham Hospital since it was founded. He was a fellow of the Massachusetts Medical Society and the American Medical Association. For a number of years he was associated with the Medical Department of the Employers Liability Assurance Corporation.

Three daughters and five grandchildren survive him.

OLEF—ISADORE OLEF, M.D., of Dorchester, died December 16. He was in his forty-sixth year.

Dr. Olef received his degree from Harvard Medical School in 1926 and at the time of his death was assistant professor of medicine at Tufts College Medical School. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and two daughters survive him.

WAR ACTIVITIES CIVILIAN DEFENSE

LESSONS FROM BRITISH EXPERIENCE IN CIVIL DEFENSE

The following circular (Medical Series No. 20) was recently sent to all regional directors and regional medical officers by Dr. George H. Bachr, chief medical officer, United States Office of Civilian Defense:

Three years of British experience with air raids have significantly modified earlier concepts regarding the field casualty services. The following observations made on a recent inspection of emergency medical facilities in England and Scotland are forwarded for your information and for transmission through state chiefs to local chiefs of Emergency Medical Services.

(1) Heavy raids occur invariably at night; heavier high-explosive bombs and land mines are now being employed, up to 2000 kg., with much greater destructive ef-

fects. Incendiary bombs are used in much larger numbers, and fire is now the most serious hazard. Daylight raids are usually hit-and-run affairs in which solitary planes participate.

(2) In large cities the field casualty services may handle 2500 to 3500 casualties during a night raid. All serious casualties are moved directly to hospitals, never to first-aid posts. Heavy raids are apt to be repeated on subsequent nights when the protective forces are exhausted.

(3) A large fleet of four-stretcher ambulances is essential for life saving. Fourteen thousand ambulances were made in England and Scotland by purchasing used cars, stripping them and then mounting a simple ambulance body on the chassis. London uses over 1500 such ambulances and 550 sitting-case cars. The use of tradesmen's trucks proved universally unsatisfactory; three out of four never arrived on the scene, and lives were lost owing to the delay and confusion. Because of the large number of casualties to be transported in a few hours, no ambulances that carry less than four stretchers are employed. For the simultaneous evacuation of damaged hospitals, a fleet of 200 converted buses carrying 10 stretcher cases and 6 to 10 sitting cases are immediately available, and another 200 are obtainable within two hours.

(4) Casualty stations (British fixed first-aid posts) are necessary at or near all hospitals and at places more than a mile from hospitals to care for minor casualties that do not require hospitalization. Many are now on a care-and-maintenance basis and are activated only during a raid. When functioning, the staff usually consists of one or two doctors, several nurses and a variable number of aides and auxiliaries.

(5) In large cities, casualty stations need not be more numerous than one per 25,000 inhabitants; they should be located about a mile apart. There are less than 300 in the London area, with a population of about 10,000,000 and a land area more than twice that of Greater New York. In smaller, thinly settled communities, they are more numerous in relation to population, but the distances between them are proportionately greater than in metropolitan cities. Many of the minor casualties are moved to first-aid posts in sitting-case cars; some walk.

(6) First-aid parties (stretcher teams) are not necessary, are a waste of manpower and are rapidly being eliminated. First aid at incidents is essentially a function of the rescue parties (rescue teams), which extricate the casualties from under the debris of demolished buildings. All first-aid parties in England and Scotland are therefore being merged into the rescue parties. They include a leader, an assistant leader and eight other members, and are entirely independent of the fire department. They are a life-saving service related to the medical services concerned in field casualty work.

(7) The experiences of Britain under air-raid conditions have dispelled many preconceived notions concerning first aid. Almost all raids occur at night; the victims are crushed under the debris of demolished buildings and are either dead or severely injured; less than a third are slightly injured and can be cared for at casualty stations; all the severely injured must go to a hospital; victims are invariably covered with dust and dirt, which hangs in the air for hours. The conditions under which the rescue workers encounter the injured beneath the structural debris, the darkness, and the dust that always fills the air, the large proportion of dead and severely injured, and the urgent need for immediate

hospitalization make it impossible to apply most peacetime concepts of first aid.

(8) Wounds are usually grossly contaminated and need only be covered with a shell dressing until the casualty reaches the hospital. Hemorrhage is usually controllable with a pressure dressing. The tourniquet is rarely employed. Burns are covered only with sterile gauze until the casualty arrives at the hospital. Tannic acid jelly as a first-aid dressing for burns has been discarded because of the dirt that invariably contaminates the burned surface, because the jelly deteriorates rapidly and, lastly, because tannic acid ignites in the presence of phosphorus when applied to burns caused by the explosion of phosphorus-oil bombs.

(9) Traction splints are not used. An exception is made if the casualty must be transported a long distance over country roads. Unlike Army field experience in the last war, the few miles of travel to a hospital over the paved roads of a city do not warrant the application of traction, especially as the darkness and the conditions of an air raid also make hurried application of the procedure difficult or impossible. All that can be done is to place the fractured extremity gently in alignment, bind it with triangular bandages to the uninjured leg or to an improvised splint, or apply a Thomas splint if one is on hand. Movement of the fragments can also be minimized by snug application of the blankets according to the Wanstead technic of blanketing and by the use of sandbags, which should always be carried in the ambulance.

(10) Shock is treated at the incident by prompt administration of adequate doses of morphine (up to $\frac{1}{2}$ gr. for adults), coramine, proper blanketing, administration of fluids, and the use of hot-water bottles during transportation to the hospital. The use of plasma or blood transfusion is deferred until arrival at the hospital; it is ordinarily quite impossible in the darkness, dirt and confusion at the incident.

(11) The presence of a physician at the incident is invaluable, but more than one is unnecessary. In fact, one physician may cover several nearby incidents, leaving his nurse or one of the nursing auxiliaries of his emergency team at the incident while he moves temporarily from one to another in the immediate neighborhood.

(12) Even though a single night's casualties requiring hospitalization may total 1000 or 2000, large hospitals rarely receive more than 50 to 100, the load being distributed as evenly as possible throughout the city.

(13) A large casualty receiving hospital is often related to one or more peripheral hospitals in the suburbs or in a country district. There are now four base-hospital beds for each casualty bed in the cities.

(14) On receipt at a local report and control center of a message from an air-raid warden that an incident and casualties have occurred, an "express party" is immediately dispatched to the scene. An "express party" includes one rescue first-aid party, one ambulance, one sitting-case car, and one mobile medical unit (mobile medical team). The latter consists of one physician, one nurse and two auxiliaries. No other equipment and personnel of the emergency medical service is dispatched unless additional assistance is requested by the incident officer (usually a higher police official) or by the incident physician on the scene. In this manner, useless movement is avoided and equipment and personnel of the community is carefully conserved.

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BRONCHIAL OBSTRUCTION AND TRACHEOBRONCHIAL TUBERCULOSIS*

EDWARD B. BENEDICT, M.D.†

BOSTON

SINCE the careful studies of Clerf,¹ Eloesser,² and Samson,^{3,4} bronchoscopy in tuberculosis has been found to be increasingly important. In the early days it was thought that this procedure would be hazardous to the tuberculous patient and might result in spreading the infection, but this has not proved to be the case. On the contrary, knowledge concerning the presence or absence of disease in the tracheobronchial tree obtained by the use of the bronchoscope has been of great aid to the internist and thoracic surgeon in planning treatment.

Tracheobronchial tuberculosis may take three principal forms: the ulcerative, in which there is a diffuse or circumscribed loss of mucosa; the hyperplastic, where there is submucosal proliferation and sometimes the formation of conglomerate tubercles; and the stenotic, in which there is definite scar-tissue formation leading to partial or complete bronchial obstruction.

The indications for bronchoscopy in tuberculosis are as follows: obstructive signs and symptoms as shown by atelectasis, wheeze, difficulty in raising sputum, persistent cough or dyspnea and intermittent febrile attacks; positive sputum when parenchymal disease is controlled or absent; hemorrhage, unexplained by parenchymal disease; and contemplated collapse therapy to determine the possible presence of tuberculosis in the trachea or contralateral bronchus.

In a previous paper⁵ I called attention to 4 cases having symptoms of intermittent bronchial obstruction following thoracoplasty, all of which were relieved by bronchoscopic aspiration of secretions with bougienage. One patient in this group later required lobectomy.

Tuberculous stricture of the bronchus following thoracoplasty may produce an almost complete

obstruction, which can often be markedly relieved by repeated bronchoscopic dilatation.

Since there are many other causes of bronchial obstruction, let us first consider the differential diagnosis. The clinical history, together with the x-ray and laboratory findings, may often lead to a correct presumptive opinion concerning the cause of bronchial obstruction, but in the last analysis only direct bronchoscopic study with biopsy of the lesion will give the final histologic diagnosis. As examples the following cases are cited.

CASE 1. G. E. H. (M. G. H. U216741), a 27-year-old man, first entered the hospital because of cough and



FIGURE 1. Case 1.

Atelectasis of right lung; presumptive diagnosis, adenoma; bronchoscopic biopsy, epidermoid carcinoma, Grade III.

hemoptysis of 10 months' duration. X-ray examination (Fig. 1) showed complete atelectasis of the right lung.

*From the Massachusetts General Hospital.
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†Instructor in surgery Harvard Medical School, associate visiting surgeon, Massachusetts General Hospital, consulting surgeon, Massachusetts Eye and Ear Infirmary.

Because of the patient's youth the presumptive diagnosis was benign adenoma of the right main bronchus. Bronchoscopy,* however, revealed a malignant tumor, which was biopsied and reported as epidermoid carcinoma, Grade III.

CASE 2. W. M. R. (M. G. H. U224885), a 56-year-old man, entered the hospital complaining of cough and hemoptysis of 1½ years' duration. X-ray examination

to a report of metastatic sarcoma. Following partial bronchoscopic removal there was temporary improvement, with some re-expansion of the left upper lobe.

Another cause of partial bronchial obstruction is sarcoid. In a case previously reported,⁶ the chief complaints were dyspnea and wheeze. The chest x-ray finding was that of sarcoid. Bron-

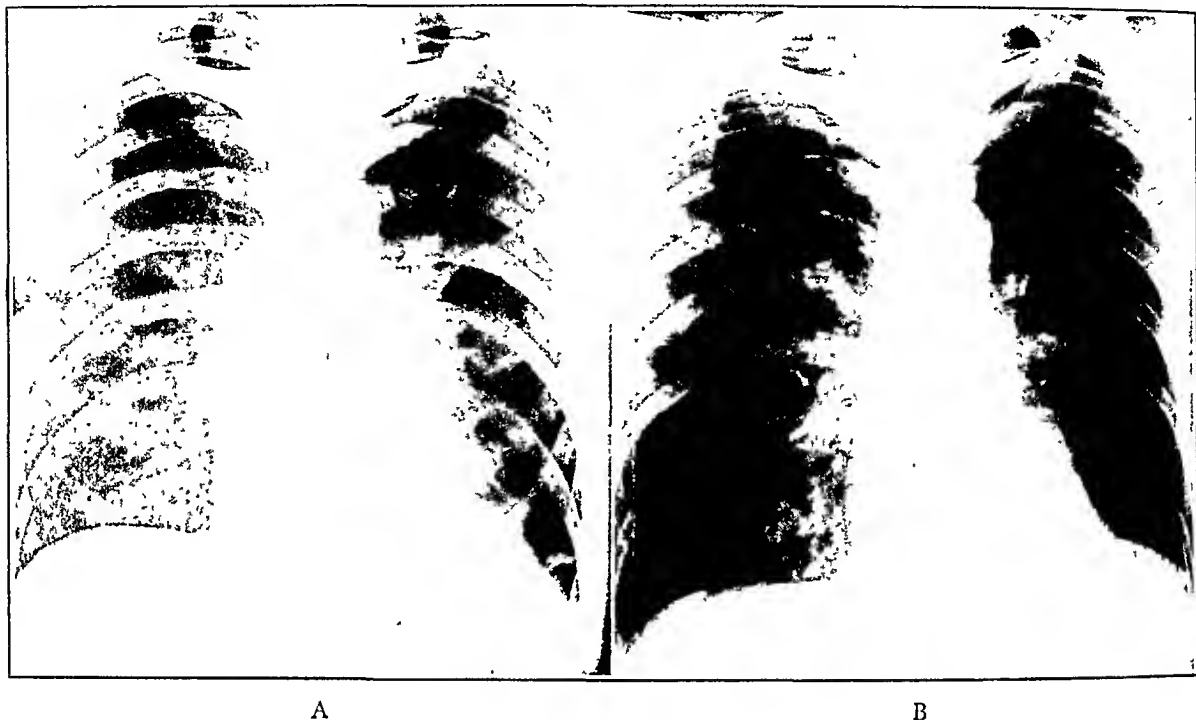


FIGURE 2. Case 2.

A—Collapse of left lower lobe, with a mass at left hilus; presumptive diagnosis, carcinoma; bronchoscopic biopsy, benign adenoma. B—Following removal of adenoma, persisting collapse of left lower lobe, without hilar shadow; patient asymptomatic.

(Fig. 2A) showed a mass in the left hilus with collapse of the left lower lobe. Because of the patient's age the presumptive diagnosis was bronchogenic carcinoma. Bronchoscopy, however, showed a smooth, round, lobulated tumor arising in the left-lower-lobe bronchus. A biopsy specimen was reported as benign adenoma. Following bronchoscopic removal the patient has remained essentially symptom free for the past 2½ years. The collapse of the left lower lobe persists but the mass in the left hilus has disappeared (Fig. 2B). The bronchoscopic appearance of the adenoma is shown in Figure 3.

A rare cause of bronchial obstruction is metastatic tumor.

CASE 3. W. C. P. (M. G. H. U30702), a 42-year-old man, first entered the hospital in 1938, at which time a sarcoma of the testicle was removed. Nine months later he was readmitted because of bronchial obstruction with collapse of the left lung. X-ray examination (Fig. 4) showed masses in the right-lung field consistent with metastatic tumor and a complete collapse of the left lung. Bronchoscopy demonstrated a ragged tumor mass obstructing the left main bronchus, a biopsy of which led

choscopy showed sarcoid involving the carina and both main bronchi, confirmed by biopsy. There was definite improvement following bronchoscopic removal of the tissue and secretions.

The following cases illustrate different manifestations of tracheobronchial tuberculosis.

CASE 4. A. R. (M. G. H. U84531), a 29-year-old woman, gave a 7 years' history of tuberculosis, with cough and positive sputum. She had had a left phrenicectomy. During the previous year there had been intermittent periods of fever, with increased cough and sputum. X-ray examination (Fig. 5) showed complete collapse of the left lung with cavitation. At bronchoscopy, almost complete obstruction of the left main bronchus 2 cm. below the carina was demonstrated. The stricture was smooth and no ulceration was seen. It was dilated by the passage of esophageal bougies (sizes 8 to 12). No follow-up was obtainable, as the patient lived at a distance.

This patient had a positive sputum, and bronchoscopy confirmed the presumptive diagnosis of tuberculous stricture.

*All bronchoscopies were performed by me except those in Cases 9 and 10, performed by Dr. Lowrey F. Davenport, and the first bronchoscopy in Case 14, performed by Dr. Ralph H. Adams.

CASE 5 C M D (M G H U346536), a 26-year-old woman, gave a long standing history of pulmonary tu



FIGURE 3 Case 2

Bronchoscopic appearance of multilobular adenoma

berculosis and tuberculous laryngitis with positive sputum. She had been treated by partial right pneumothorax and left oleothorax. X-ray examination (Fig 6) showed the



FIGURE 4 Case 3

Atelectasis of left lung due to occlusion of bronchus metastatic from testicle metastatic disease also in right lung field

right lung half collapsed and herniated across the midline. There was oil on the left side and possible partial occlusion of the left main bronchus. At bronchoscopy the

left main bronchus 2 cm below the carina was narrowed to 1-3 mm lumen. The stricture was smooth and fibrous. It was dilated by the passage of esophageal bougies (sizes 12 to 16). There were no retained secretions. A smear taken from the stricture showed tubercle bacilli.

CASE 6 A W P (M G H U329952), a 38-year-old man, entered the hospital because of chronic cough and positive sputum. X-ray examination (Fig 7) showed partial collapse of the right upper lobe, with probable cavitation and stenosis of the right upper lobe bronchus. Bronchoscopy demonstrated reddening and almost complete stenosis of the right upper lobe bronchus, with two pinpoint tubercles (Fig 8). The stenosis was best seen in the use of the right-angle telescope¹⁸ (Fig 9). Since the disease was confined to the right upper lobe and re-



FIGURE 5 Case 4

Atelectasis of left lung positive sputum tuberculous stricture of left main bronchus

parable damage to this lobe had already occurred, lobectomy was performed by Dr E. D. Churchill, with success. The pathologic specimen showed no cavitation but moderate bronchiectasis, with very extensive microscopic bronchial tuberculosis throughout the lobe. The patient made a satisfactory recovery and has been essentially symptom free for 7 months since the operation.

In the above 3 cases positive sputum for tuberculosis made the diagnosis fairly obvious. In some of the following cases, however, the sputum was negative and the diagnosis was more obscure.

CASE 7 V D (M G H U253261), a 28-year-old woman entered the hospital complaining of cough, fever and chills of 1 year's duration. The sputum had been negative for tubercle bacilli on ten examinations. X-ray examination (Fig 10) showed calcified lymph nodes and collapse of the right lower lobe. The X-ray Department made a tentative diagnosis of tuberculosis in spite of the negative sputum. Bronchoscopy revealed distortion of

the right bronchial tree with outcropping near the bifurcation of the lower lobe. The biopsy diagnosis was tuberculosis. Pneumonectomy was later performed by Dr. Richard H. Overholt.

CASE 8. M. L. K. (M. G. H. U271988), a 59-year-old man, entered the hospital because of recurrent attacks of hemoptysis. The sputum on several occasions had been negative for tuberculosis. X-ray examination (Fig. 11) showed probable tuberculosis of the left upper lobe, with bronchiectasis. Bronchoscopy, however, revealed a 7-mm ulcer of the right stem bronchus, the ulcer having sharp margins and a dirty base. A smear taken from the ulcer was positive for tuberculosis. A year and a half later

cluded by a red, elevated, fungating mass, from which a biopsy was obtained, the pathological report being tuber-

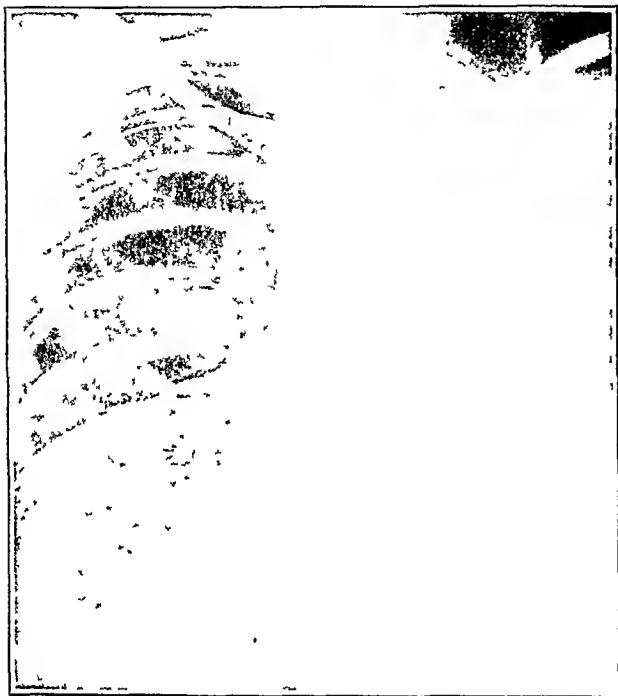


FIGURE 6. Case 5.

Partial collapse of right lung, with pneumothorax, herniation of right lung across the midline, left pleurothorax, positive sputum, tuberculous stricture of left main bronchus.

the patient's physician reported that he was getting along satisfactorily under medical care.

It is noteworthy in this case that most of the disease was assumed to be in the left upper lobe, but bronchoscopy showed an active, ulcerating lesion in the right stem bronchus. Information of this sort is naturally of very great importance, especially if any surgical treatment is contemplated. Moreover, bronchoscopy in this case, as in Case 7, was the only method of examination to yield a positive diagnosis.

CASE 9. T. F. (M. G. H. U205925), a 28-year-old woman, entered the hospital with a 3-year history of cough, fever and wheeze. Left pneumothorax had been necessary every 6 weeks. Tubercle bacilli had never been found in the sputum on repeated examinations. X-ray examination (Fig. 12) showed complete collapse of the left lung, with cavity formation. Bronchoscopy demonstrated that the left main bronchus was completely oc-



FIGURE 7. Case 6.

Partial collapse of right upper lobe, with cavitation, positive sputum.

culosis. Eight months later a second bronchoscopy showed the left main bronchus almost completely stenosed and represented by only a small dimple in the mucous mem-



FIGURE 8. Case 6.

Bronchoscopic appearance of right-upper-lobe orifice as seen with right-angle telescope; almost complete stenosis of orifice, with two pin-point tubercles just proximal to the stenosis.

brane of the trachea. There was no evidence of tuberculosis in the trachea or right main bronchus. Accordingly, Dr. Churchill performed a left pneumonectomy. Unfortunately, however, in spite of all precautions taken, the

disease progressed in the right lung and the patient died 1½ years later.

Cases 7, 8 and 9 illustrate the importance of bronchoscopy in establishing a positive diagnosis of

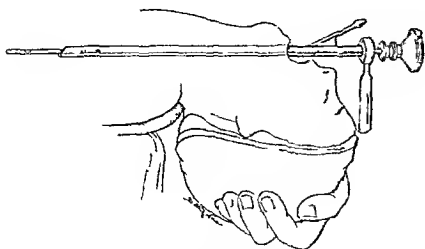


FIGURE 9

Diagram showing technique of introducing telescope with right angle vision through a small tubular bronchoscope for inspection of upper lobes.

tuberculosis when all sputum examinations have been repeatedly negative.

CASE 10 J J McC (M G H 46818) 43 years old man, entered the hospital with a 20 year history of cough

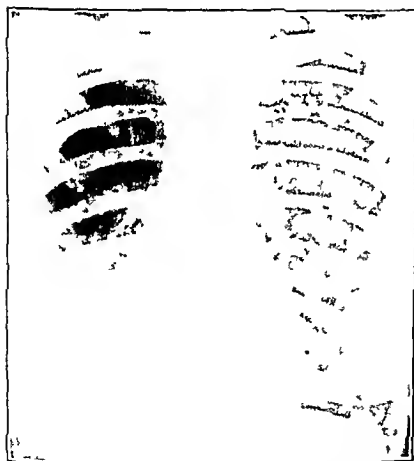


FIGURE 10 Case 7

Atelectasis of right lower lobe with calcified lymph nodes, negative sputum, bronchoscopic biopsy tuberculosis of right lower lobe bronchus.

and a 6 month history of hemoptysis. Sputum was expectorated up to a cupful each day and had several times been positive for tuberculosis. X-ray examination (Fig 13) showed a mass at the right hilus, with cavitation. Because of the positive sputum tuberculosis was

considered likely although carcinoma was also mentioned. Bronchoscopy revealed an irregular fungating mass near



FIGURE 11 Case 5

Probable tuberculosis of left upper lobe, negative sputum, bronchoscopic examination, 1 mm ulcer of right stem bronchus, bronchoscopic smear from ulcer positive.

the right middle lobe since the final diagnosis was epidermoid carcinoma Grade IV. Pneumonectomy was



FIGURE 12 Case 9

Atelectasis of left lung, sputum negative, bronchoscopic examination, fungating mass in left main bronchus, bronchoscopic biopsy tuberculosis.

therefore performed by Dr. Churchill. Five years later the patient was fairly comfortable although complaining of some dyspnea and cough.

In this case clinical evidence pointed chiefly to tuberculosis, but bronchoscopy disclosed a bronchogenic carcinoma in addition to the tuberculosis.

CASE 11. M. E. W. (M. G. H. U189707), a 57-year-old woman, entered the hospital complaining of wheeze of 2



FIGURE 13. Case 10.

Right hilar mass, with cavitation; positive sputum; bronchoscopic biopsy, epidermoid carcinoma, Grade IV.

months' duration. There was almost no cough or sputum. Sputum examinations on several occasions were negative

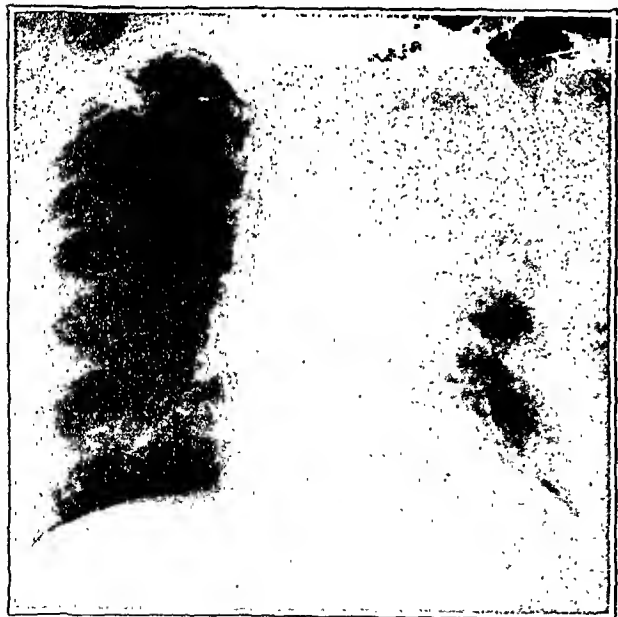


FIGURE 14. Case 11.

Atelectasis of left upper lobe; partial atelectasis of left lower lobe; sputum negative; bronchoscopic examination, multiple tubercles in left main bronchus; bronchoscopic aspirations, positive in guinea pig.

for tuberculosis. X-ray examination (Fig. 14) showed complete collapse of the left upper lobe and partial col-

lapse of the left lower lobe. The findings were interpreted as being possibly due to carcinoma, although the pointed extremity of the left main bronchus and numer-

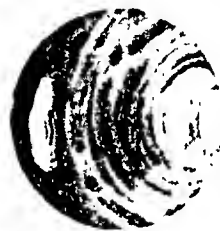


FIGURE 15. Case 11.

Bronchoscopic appearance of multiple tubercles in left main bronchus, showing left-upper-lobe orifice and subdivisions of left lower lobe.

ous calcified glands raised the possibility of a benign tuberculous stricture. Bronchoscopy (Fig. 15) showed multiple tubercles extending down the left main bronchus all the way from the carina to the partial stenosis. A



FIGURE 16. Case 12.

Atelectasis of right lower and right middle lobes (portable film); clinical diagnosis, bronchogenic carcinoma with brain metastases; bronchoscopic biopsy, acute and chronic inflammation (? tuberculosis); subsequent sputum positive.

guinea pig inoculated with bronchoscopic aspiration developed tuberculosis. X-ray treatment was given, with definite improvement. Three years later the patient re-

ported no further upsets, no cough, negative sputum and some wheeze. X-ray examination showed fibrosis of the left upper lobe.

In this case bronchoscopic examination resulted in a positive diagnosis of tuberculosis, for which X-ray treatment was subsequently given.

CASE 12. B. F. (M. G. H. U235515), a 62-year-old woman, entered the hospital complaining of 2 years' wheezing, 4 days' fever and 1 day's drowsiness and headache. Thirty years previously she had had pleurisy with effusion. Otherwise there was nothing to suggest tuber-

culosis (Fig. 17) showed an upper right seven-rib thoracoplasty. Because of persistent cough, positive



FIGURE 17. Case 13.

Upper right thoracoplasty, followed by persistent cough, positive sputum and wheeze; bronchoscopic examination, multiple tubercles in right main and right stem bronchi; later, complete stenosis.

culosis. X-ray examination (Fig. 16) showed collapse of the right lower and right middle lobes (portable film). A chest consultant decided that the probable diagnosis was bronchogenic carcinoma with brain metastases. Bronchoscopy, however, disclosed a nodular lesion of the right stem bronchus with central necrosis. The gross appearance was consistent with carcinoma. The biopsy diagnosis was acute and chronic inflammation, with necrosis and possible tuberculosis. The sputum subsequently was positive for tuberculosis. Two years later the patient was making a slow but constant improvement on medical management.

This case is the reverse of Case 11, as here the probable clinical diagnosis was carcinoma, but bronchoscopy showed tuberculosis.

CASE 13. J. G. (M. G. H. U153402), a 46-year-old woman, gave a history of right phrenicectomy for tuberculosis 2 years before entry. One year previously she had undergone a two-stage thoracoplasty, followed by persistent cough, positive sputum and wheeze. X-ray exami-



FIGURE 18. Case 14.

Fibrosis and calcification of left lung, following first-stage thoracoplasty for tuberculosis, persisting positive sputum, bronchoscopic examination, tuberculous stricture of left main bronchus, later, successful pneumonectomy.

sputum and wheeze, bronchoscopy was performed, disclosing the right-upper lobe orifice collapsed and the right main and stem bronchi studded with tubercles. Two



FIGURE 19. Case 14.

Low-power cross section of bronchus, showing markedly reduced lumen.

months later bronchoscopy was repeated and the process was found to be more advanced, with stenosis of the right stem bronchus and involvement of the left main bronchus. Two years later on a medical regimen there was still moderate cough but less wheeze, and some slow improvement.

Bronchoscopy in this case demonstrated the presence of active tracheobronchial tuberculosis following thoracoplasty.

CASE 14. H. V. (M. G. H. U295413), a 42-year-old woman, entered the hospital complaining of left-sided

tive diagnosis was carcinoma of the esophagus, with involvement of the recurrent laryngeal nerve and invasion of the tracheobronchial tree. Esophagoscopy, however, showed a normal esophageal mucosa with evidence of extrinsic pressure. Bronchoscopy revealed an extensive proliferative mass involving the left main bronchus, the



FIGURE 20. Case 15.

A—Upper mediastinal mass in patient with cough, hoarseness and dysphagia. B—Apparent destruction of esophageal mucosa; presumptive diagnosis, carcinoma of esophagus; esophagoscopy, negative; bronchoscopic biopsy, bronchial tuberculosis.

wheeze and positive sputum associated with pulmonary tuberculosis of the left lung. Bronchoscopy prior to entry had shown an ulcer of the left main bronchus. Bronchoscopy showed narrowing of the left main bronchus in the region of the left-upper-lobe orifice. There was no evidence of activity. The appearance was that of a healed bronchial ulcer. A first-stage thoracoplasty was undertaken, followed by persistent wheeze. A second bronchoscopy, 6 months later, revealed a stricture of the left main bronchus just above the left upper lobe. The positive sputum persisted. X-ray examination (Fig. 18) showed fibrosis and calcification. A third bronchoscopy, 5 months later, again demonstrated stricture of the left main bronchus 2 cm. below the carina. There was no ulceration, and the lumen was only 3 cm. in diameter. Pneumonectomy was therefore performed by Dr. Churchill. The postoperative course was satisfactory and 3 months later the patient was reported as doing well. The reduced lumen of the left main bronchus is shown in a low-power cross section in Figure 19.

CASE 15. A. J. P. (M. G. H. U328726), a 38-year-old man, entered the hospital complaining of cough of 13 months' duration, hoarseness for 11 months and dysphagia for 5 weeks. Mirror laryngoscopy showed the left vocal cord to be paralyzed in the midline. X-ray examination (Fig. 20A) revealed a mass in the upper mediastinum, with narrowing of the esophagus and apparent destruction of the esophageal mucosa (Fig. 20B). The presump-

carina and the right main bronchus. The tissue removed at the time of bronchoscopy was reported as showing evidence of tuberculosis.

This is obviously a very unusual case, for several reasons. Paralysis of a vocal cord is common in malignancy but rare in tuberculosis. The dysphagia appeared to be the presenting symptom but was apparently overemphasized, for the cough and hoarseness preceded it. However, most of the clinicians concluded that there was a probable malignancy of the esophagus. Bronchoscopy and esophagoscopy demonstrated the true nature of the process.

CONCLUSIONS

Among the most frequent causes of bronchial obstruction are carcinoma, benign tumor and tuberculosis.

The clinical picture may lead to an erroneous presumptive diagnosis, for the underlying cause of the obstruction frequently cannot be determined by laboratory and x-ray studies.

Bronchoscopy with biopsy or smear is necessary to establish a positive diagnosis.

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THE USE OF SULFADIAZINE IN THE MANAGEMENT OF SIMPLE MASTOIDECTOMY WOUNDS

LIEUT CHARLES A TUCKER, MC, AUS,* AND MAJOR CARLYLE G FLAKE, MC, AUS†

BOSTON

IN SEPTEMBER, 1941, Livingston,¹ of Chicago, reported a series of 13 cases in which sulfonamide drugs were used locally in mastoid cavities, the wounds being closed without drainage. The results were remarkable in that the postoperative course was greatly shortened. Apparently, this was the first report of the local use of sulfonamide drugs in mastoidectomy wounds, although they had previously been used in the treatment of compound fractures and peritonitis, as is well known.

The primary closure of mastoidectomy wounds without drainage was not new. Near the turn of the century it was a common practice among reputable otologists to close the wound after it had been allowed to fill with a blood clot—the so-called “blood clot method.” Sprague² and Reik³ among others, reported considerable success. They described how the blood clot became organized and filled in by the growth of fibroblasts and osteoblasts. This method fell into disuse, however, because it was quite unsuccessful in the hands of many surgeons; the clot frequently broke down, and the wound opened and subsequently healed by the slow process of granulation. Nevertheless, otologists were influenced to the extent that, instead of packing the mastoid wounds wide open, a method was devised whereby a drain was inserted in the cavity and the wound closed except at the site of the drain. This procedure has been generally employed up to the present day.

From the results of Livingston's report, however, one might assume that local chemotherapy would exert a sufficient bacteriostatic or bactericidal effect to make a primary closure feasible in a high percentage of cases. Yet there remained a reasonable doubt concerning the validity of his results, since these cases, as reported, were not controlled.

With this latter point in mind, we studied a series of controlled cases in which operation was per-

formed at the Children's Hospital from October, 1941, through June, 1942. The present report is a summary of observations from these cases.

All cases were those in which the present illness was six weeks or under in duration and in which no sulfonamides had been given before hospital admission. The period of six weeks was a purely arbitrary one which, for the purpose of simplicity, we called the stage of acute mastoiditis. The series was then divided into three parts. Group A comprised those cases in which sulfadiazine⁴ was placed directly in the mastoid wound at the close of operation and the wound was sutured without drainage. No sulfonamides were given by mouth. The Group B cases received sulfadiazine by mouth, both preoperatively and postoperatively, and the wound was sutured without drainage, no sulfadiazine being given locally. The Group C cases received no sulfonamide, either by mouth or within the wound, which wound was drained at the lower pole by a small wick of gutta percha gauze.⁵

These cases were taken in rotation, Case 1 being placed in Group A, Case 2 in Group B, Case 3 in Group C, Case 4 in Group A, and so on. With the series controlled in this fashion, we hoped to rule out certain errors. First, the year to year variation in the severity of acute mastoiditis and its sequelae would be obviated. Secondly, there was a strong possibility that the level of sulfadiazine in the blood stream might be a factor in rapid healing. Sulfadiazine levels, in those who received sulfadiazine by wound only, showed values as high as 15 mg per 100 cc of whole blood, although in most cases the level was 1 mg per 100 cc or less. The level five days postoperatively was usually less than 1 mg per 100 cc.

⁴The sulfadiazine used in this series was kindly supplied by the Lederle Laboratories, Pearl River, New York.

⁵Another group is readily apparent for its control value in which the wound is closed without drainage and without sulfonamides. This procedure was not undertaken since we did not believe that it would prove to be of sufficient value to subject the patient to the necessary risk.

*Formerly assistant otolaryngologist, Children's Hospital and Junior Association, Boston; later at Brigham Hospital.

†Assistant in surgery, Harvard Medical School and visiting otolaryngologist at Children's Hospital (on leave of absence).

TECHNIC

Group A

A complete simple mastoidectomy was performed in each case in Group A. Care was taken to enlarge the aditus ad antrum, so that in most cases the short process of the incus was exposed. In some cases this was obscured by granulation tissue. After the mastoid bone had been exenterated, the cavity was flushed with warm physiologic saline solution. A piece of gauze dampened with a 1:1000 solution of epinephrine was then placed in the cavity and interrupted periosteal sutures were taken with No. 0 or 00 plain catgut, but not tied. The pack was then removed and sulfadiazine powder was poured into the cavity from a sterile test tube. The periosteal sutures were tied. No attempt was made to pack the light, fluffy powder into the cavity. Some of the powder was dusted freely into the subcutaneous regions and along the skin edges. The skin was then closed with interrupted black-silk sutures, using the Poole mattress stitch. No pack was placed within the external auditory canal. From 0.5 to 2.0 gm. of sulfadiazine was used in each case, depending on the size of the cavity. The sulfadiazine had been previously autoclaved in cotton-stoppered test tubes at 270°F. for ten minutes. The adenoids were removed following mastoidectomy whenever they were found to be hypertrophied by palpation, roentgen examination or nasopharyngoscopy. Dressings were usually done on the second postoperative day, at which time it was possible to replace the bulky dressing applied at operation with a small postaural piece of gauze. Sutures were removed on the sixth to the eighth postoperative day. The ear canal was kept free of discharge by wiping with dry cotton swabs every four hours as long as needed.

Group B

A similar operation with closure was performed in Group B, the chief difference being that the sulfadiazine was not used locally, but instead was given by mouth for one day preoperatively and for seven to ten days postoperatively, in amounts sufficient to produce a blood level of 10 to 15 mg. per 100 cc. Postoperative dressings were essentially the same.

Group C

The operation in Group C was similar to that in Groups A and B. The wound was closed as in the first two groups, except at the inferior pole, where a gutta-percha gauze wick was inserted, extending up to the antrum. This wick was replaced on the second postoperative day by a small piece of rubber tissue, which was removed and re-

inserted every other day until drainage was minimal, at which time the wound edges at the lower pole were allowed to seal over.

ANALYSIS OF RESULTS

Group A

The number of patients in Group A, in which sulfadiazine was used locally and the wound was sutured, was 16 and the number of cases of mastoiditis operated on 22, there being 6 cases of bilateral mastoidectomy. Of these 6, 2 cases deserve special mention. In one, the wound was closed on the right with sulfadiazine and drained on the left without sulfadiazine. The results here were entirely opposite from the remainder of the series, in that the drained ear ceased to discharge on the ninth postoperative day and the wound was healed on the seventeenth postoperative day, whereas the undrained ear discharged for thirty-three days. In another case, treated similarly, the undrained side healed in eight days, the drained side in twenty-four days.

In all, twenty operations were performed in which sulfadiazine was placed within the wound. All the wounds healed per primam. There were no complications, with the exception of one case that developed a subcutaneous postaural abscess on the eighteenth postoperative day, necessitating incision and drainage, with healing complete four days later. These cases, along with the other two groups, are summarized in Table 1.

Bacteriologic findings. Sixteen wounds showed beta-hemolytic streptococcus in pure culture, 1 showed beta-hemolytic streptococcus and *Staphylococcus aureus*, and 1 *Haemophilus influenzae*. The cultures from 2 wounds showed no growth.

Pathologic changes. All removed tissue revealed pus, granulations or necrosis, alone or in combination. One case had a large subperiosteal abscess, which extended up to the temporal region, causing trismus.

Age. The children varied from nine months to six years and eleven months in age.

Follow-up. This was carried out on every patient and varied from three weeks to six months. One patient developed a postaural abscess after six months, which healed without event. This was the only recurrence of mastoid-cavity infection.

Hospitalization and drainage. The average length of aural drainage was 10.0 days. The average length of time required for both the wound and middle ear to heal, including complications, was 10.1 days.

Group B

The number of patients in Group B, in which sulfadiazine was given by mouth and the wound

was closed, was 15, and the number of operations for mastoiditis 18. Of these, 1 patient had a bilateral mastoidectomy in which the right wound was sutured and the left was drained. Both ears

Follow-up. This varied from one week to four months. There was no recurrence of ear infection.

Hospitalization and drainage. The average length of aural drainage was 8.2 days. The average

TABLE 1 Data on the Three Groups of Patients

DATA	GROUP A	GROUP B	GROUP C
Number of patients	16	15	15
Number of ears operated on	20	17	16
Age incidence	9 mo to 6 yr 11 mo	10 mo to 8 yr 8 mo	5 mo to 6 yr 4 mo
Wound healing	Per primam	1 per primam except for 2 cases	Healing complete in 3 wk (11 cases)
Average days of aural discharge	10.0	8.2	Over 15 days
Bacteriology (operative wound culture)	16 beta hemolytic streptococcus 1 beta hemolytic streptococcus and <i>Staph. aureus</i> 1 <i>H. influenzae</i> 2, no growth	5 beta hemolytic streptococcus 1 pneumococcus, 1 gram positive rods 10 no growth	10 beta hemolytic streptococcus 1 beta hemolytic streptococcus and <i>Staph. aureus</i> , 1 pneumococcus, 4 no growth
Complications	1, subcutaneous postaural abscess on 18th postoperative day	1 wound broke down 1, wound became infected 1 wound developed stitch abscess	1 subcutaneous wound infection with healing by secondary intention 1 cavity revised after 4 wk 4 cavity revised after 7 wk
Average days of hospitalization	10.0	9.0	Over 21

ceased to discharge in six days. The right wound healed per primam. The left healed entirely except at the drain site, where final healing occurred on the fifteenth postoperative day.

In all, 17 mastoid processes were operated on by this method. Of these, 15 healed per primam. One developed a subcutaneous wound infection on the fifth day, which healed by the tenth day. In another case, a bilateral mastoidectomy, the left postaural wound broke down and had to be re-sutured. Final healing took place on the twentieth postoperative day. Two cases had small stitch abscesses.

Bacteriologic findings. Cultures from the mastoid processes showed beta-hemolytic streptococcus in 5 wounds, pneumococcus (not typed) in 1, gram-positive rods (not identified in 1), and no growth in 10. This is a large number of negative cultures, explained perhaps by the fact that sulfadiazine was given by mouth preoperatively. The ears on admission showed a much greater number of positive cultures for pathogenic organisms, only 3 being nonpathogenic.

Pathologic changes. All removed tissue revealed pus, granulations or necrosis, alone or in combination. In one case there was a definite perisinus abscess, and in another granulations were present on the sinus. One case developed a subperiosteal abscess.

Age. The children varied from ten months to eight years and eight months in age.

of the time for both the wound and middle ear to heal, including complications, was 90 days

Group C

The number of patients in Group C, in which no sulfadiazine was given and the wound was drained, was 15, and the number of mastoid processes operated on 16. Of these patients, 10 had an uneventful convalescence. In 1 case, the wound edges separated and healed by secondary intention. In 4 cases, the mastoid cavities were revised after five to seven weeks of drainage.

Bacteriologic findings. Of the cultures from mastoid wounds, 10 showed beta-hemolytic streptococcus, 1 showed beta-hemolytic streptococcus and *Staph. aureus*, 1 pneumococcus (not typed), and 4 no growth.

Pathologic changes. All removed tissue revealed pus, necrosis or granulations, alone or in combination. Two cases showed subperiosteal abscesses.

Age. These children varied from five months to five years and four months in age.

Follow-up. This ranged from one week to six months. Two cases showed recurrent aural discharge, 1 as a result of measles. Both cases healed uneventfully. One case was reoperated on after five weeks and 3 after seven weeks of continued wound or ear drainage. Ordinarily, these might have been allowed to drain considerably longer. It is interesting to note that 3 patients were infants under one year of age with poor nutrition.

Sulfadiazine was used at the second operation, with prompt healing, in 3 of the 4 reoperated cases.

Hospitalization and drainage. The length of time of aural discharge averaged 15 days, and wound healing averaged 3 weeks, except for the 4 cases that were revised. In these, the convalescence was considerably prolonged.

DISCUSSION

On final analysis, the results obtained in this series of mastoidectomies seem to be significant. Although the number of cases in each group is quite small, the startling differences in the postoperative courses at least warrant further study. Study of postoperative audiograms would be of considerable interest in the final evaluation of our results, but this was not particularly feasible since all the patients were children. However, it was our impression that the hearing was not altered appreciably in those with sulfonamide therapy, since these children have had, after six weeks at the most, normal tympanic membranes and no marked loss of hearing by cursory examination.

The choice of any one of the sulfonamides in preference to others is still an open question. Sulfanilamide has been advocated for use locally because of its high solubility. However, the solubility seems to be relatively unimportant, provided that the opening into the middle ear is enlarged. In this way, the cavity decompresses itself. In most of our cases, we recovered sulfadiazine crystals suspended in the serous aural discharge. Perhaps the lesser soluble substance has a more prolonged local action. It is the opinion of one of us (C. A. T.) that a combination of sulfanilamide and sulfadiazine placed within the wound, with small amounts of sulfadiazine given by mouth postoperatively, may be the method of choice. The specificity of the sulfonamide drug used locally probably does not enter into the picture, since, at the concentrations developed locally, all these drugs have a broad bacteriostatic coverage.

Postoperative ear cultures obtained in some of the cases in Groups A and B often showed the offending organism to be present until the ear ceased to discharge. In 2 cases, it was necessary to permit the escape of serum, which had collected beneath the wound. These cases showed a mini-

mal amount of aural discharge, indicating a block, probably in the region of the aditus.

The method of wound closure is still an open question. Guerry and Putney⁴ have reported a series of controlled cases in which a sulfathiazole gauze pack was used. Their results, too, showed a remarkable improvement in postoperative convalescence.

In our series, those who received the sulfonamide by mouth did about as well as those who received it locally. The major difference, however, was in wound healing, which was definitely improved when sulfadiazine was used locally.

SUMMARY AND CONCLUSIONS

A controlled series of 41 cases of simple mastoidectomy is presented, divided into three sets as follows: Group A, those receiving sulfadiazine locally, the wound being closed without drainage; Group B, those receiving sulfadiazine by mouth, the wound being closed without drainage; and Group C, those not receiving sulfadiazine, the wound being drained in the usual fashion.

The hospitalization required in Groups A and B averaged around ten days, the wounds healing per primam and the tympanic membrane being healed and dry at that time. The wound broke down, in only 1 case, in Group B. There were no untoward results. The patients in Group C had the usual prolonged convalescence.

At this time, we cannot advocate with impunity any one method for the control of wounds in mastoidectomy, although sulfonamide therapy seems to be of definite value. Certainly the prime requisite for good results is the performance of a standardized, thorough, simple mastoidectomy.

This report, based on relatively few cases, is presented for the objective data that it contains. When it is taken together with other similar reports, which will undoubtedly appear in the literature, the correct procedure for the control of mastoidectomy wounds will eventually arise.

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CHRONIC MILIARY TUBERCULOSIS

Report of a Case

EDWARD JAMES WELCH, M.D.*

BOSTON

IN 1937, Hoyle and Vaizey¹ published their monograph on chronic miliary tuberculosis, presenting 120 cases collected from the literature and from their own experience. Since the publication of their book, several additional cases have been reported. These reports have served to demonstrate the benign course that may be followed by a disease that only recently was considered to be invariably fatal.

AGE INCIDENCE

Chronic miliary tuberculosis has been recorded at almost all ages, from the first to the seventieth year of life. The majority of cases occur in the second, third or fourth decade. Distribution between the sexes is approximately equal. An insignificant number of patients give a history of tuberculosis. Other previous illnesses and family histories of tuberculosis have a questionable influence on the incidence.

SYMPTOMS AND SIGNS

In most cases the onset is insidious, with slight symptoms and signs. Cough, expectoration and dyspnea are the commonest pulmonary symptoms, and these are usually mild. In some cases a cold dates the onset of the disease. Loss of weight and weakness are frequent constitutional complaints. Symptoms of extrapulmonary tuberculosis first bring some cases under observation.

The physical signs are inconstant. Slightly over half the cases present wasting and fever, the latter usually of mild degree. The commonest abnormal physical signs are those in the lungs, but even these are absent in one fifth of the cases. The pulmonary findings vary from localized evidence of infiltration to signs of generalized pulmonary involvement. Of the extrapulmonary signs, splenic enlargement and lymphadenopathy predominate. A small number of cases present evidence of tuberculosis of the bones or joints.

RADIOLOGIC FINDINGS

The only constant objective finding of chronic miliary tuberculosis is the typical appearance of the pulmonary lesions in roentgenograms of the chest. In all except a few cases the distribution is bilateral,

with total pulmonary involvement. In addition to the usual small, soft, ill defined lesions, occasional larger areas of infiltration or excavation are seen. The roentgenographic picture is in most cases indistinguishable from that of acute miliary tuberculosis.

Sayé² has described a nonapparent form of chronic miliary tuberculosis, which he detected in over 5 per cent of students examined radiologically at the University of Barcelona. These cases exhibited fine linear and nodular shadows in the lung fields. The significance of the lesions was to be determined by subsequent examinations. As yet no confirmatory series of similar cases has been reported elsewhere.

LABORATORY DATA

A bacteriologic diagnosis can be established in about half of all cases, and a histologic diagnosis in an additional small percentage (15 to 20 per cent) during life. Necropsy establishes the diagnosis in another 10 per cent, although even here the tubercle bacillus is often not demonstrated. Altogether, there remain about one fifth of all cases without bacteriologic or histologic evidence to support the diagnosis. In this group, the symptoms, physical signs, typical roentgenographic findings and clinical course warrant the diagnosis.

The tuberculin test has been reported in only a few cases, and in some has been negative. The failure to find the tubercle bacillus and the presence of a negative tuberculin test, even where the histologic findings are consistent with tuberculosis, leave room for doubt concerning the accuracy of the diagnosis. The close resemblance of chronic miliary tuberculosis to Boeck's disease has undoubtedly led to the improper classification of many cases.

CLINICAL COURSE

Where to draw the line between acute and chronic miliary tuberculosis is difficult to decide. Hoyle and Vaizey¹ considered that chronic cases should present a clinical course of at least three months. They found that of 64 patients sufficiently observed, 13 died within six months, 33 died within eight years (with an average length of life of two years from the date of onset of symptoms), and 18 lived to be considered arrested cases. In

*Assistant in medicine, Boston University School of Medicine, acting chief of staff, Channing House for Tuberculosis, Boston.

those who died, tuberculous meningitis and acute generalized tuberculosis were the leading causes of death. In those who lived to be followed by serial roentgenograms, the lesions appeared stationary in some, became more discrete or calcified in others, and actually disappeared in a few. The reported cases have been too few to offer reliable criteria for predicting the course of the individual patient.

MORBID ANATOMY

In those cases that have come to autopsy, the pulmonary lesions have been most constant. Except in cases terminating with an acute generalized spread of the disease, extrapulmonary lesions have not been frequent. In the lungs, numerous evenly distributed, tiny, gray or white, fibrous miliary foci, sometimes calcified, appear. Rarely are the lesions more than a few millimeters in diameter. Histologically the lesions are characterized by a great amount of fibrous tissue and by scant cellular infiltration in which giant cells and epithelioid cells predominate. Caseation has been unusual.

There has been much argument about the mode of spread of this disease. It is conceivable that a tuberculous lesion erodes the thoracic duct or a blood vessel and discharges tubercle bacilli into the blood stream. Whether a generalized systemic distribution of lesions or a restricted pulmonary distribution occurs depends on whether the channel involved is a part of the greater or lesser circulatory system. This concept of a hematogenous route of dissemination has met with greater popularity than that of a lymphogenous one. That the latter may occur, however, has been well demonstrated by Hoyle and Vaizey in the pathologic findings in one of their cases. The possibility of a bronchiogenic mode of spread must also be recognized, although a uniform dissemination of lesions throughout both lungs by this route would hardly be expected.

DIAGNOSIS

The more usual conditions offering difficulty in the differential diagnosis of chronic miliary tuberculosis are Boeck's disease, generalized carcinomatosis, pneumoconiosis and pulmonary congestion. The exclusion of rare conditions such as fungus infections, periarteritis nodosa and Hodgkin's disease may also present difficulty.

Boeck's disease is often hard to exclude. So closely alike may it and chronic miliary tuberculosis appear, that some clinicians believe both terms to refer to the same disease. A negative tuberculin test, the absence of tubercle bacilli and the presence of characteristic bone lesions in the phalanges are points in favor of the diagnosis of Boeck's disease. Even at necropsy it is often difficult to

differentiate these conditions. Snapper and Pompen³ consider that the absence of tubercle bacilli and of caseation distinguishes Boeck's disease from chronic miliary tuberculosis.

Generalized carcinomatosis may be differentiated by extreme dyspnea, the absence of tubercle bacilli and a rapidly fatal course. There is often an additional history of pain in one or more bones, leading to the discovery of other metastases.

Pneumoconiosis is excluded by the absence of a history of dust exposure.

In pulmonary congestion the preponderance of the opacities and physical signs about the hili and bases of the lungs should serve to indicate this diagnosis. An abnormal size or shape of the heart would also be suggestive.

Proof of the diagnosis of chronic miliary tuberculosis rests, during life, on finding the tubercle bacillus; after death, on finding the characteristic histologic lesions. The bacilli may be found in the sputum or in the extrapulmonary lesions. In a number of cases neither a bacteriologic nor a histologic diagnosis is possible and it becomes necessary to rely on serial roentgenography and the clinical aspects of the case. In the case reported below the diagnosis rested on these two factors alone from 1939 to 1942, when the patient developed a cavity and a positive sputum. The presence of pericarditis with effusion at one time in the course of the disease lent additional weight to the probability of a miliary tuberculous process. No case of chronic miliary tuberculosis with pericardial effusion has, to my knowledge, been recorded before.

TREATMENT

As in all degrees of pulmonary tuberculosis, treatment consists of rest and general hygienic and nutritional care. In a few cases with localized areas of infiltration or excavation, unilateral pneumothorax has been successful in controlling the disease. Partial bilateral pneumothorax has been recommended, but remains untried. Sayé² thought that some of his patients were benefited by injections of Sanocrysin.

CASE REPORT

A. S., a 58-year-old Greek tanner, was admitted to the Middlesex County Sanatorium on July 26, 1939. The past history was irrelevant. There was no history of contact with tuberculosis or exposure to silica-containing dust.

The patient was well until 4 or 5 years before admission, when he first experienced dyspnea on exertion and slight swelling of the ankles in the afternoon. Easy fatigability was sufficient to necessitate stopping work. Intermittent aching in the right side of the chest and a slight cough began at that time, and he began to raise an ounce of thick yellow sputum per day.

The patient tolerated these symptoms, however, and it was not until 15 months before admission that he consulted a physician. At that time his chief complaint

complaint was, as before, a burning pain in the epigastrium. A roentgenogram showed slight clearing of the pleural reaction on the left. He reentered the hospital

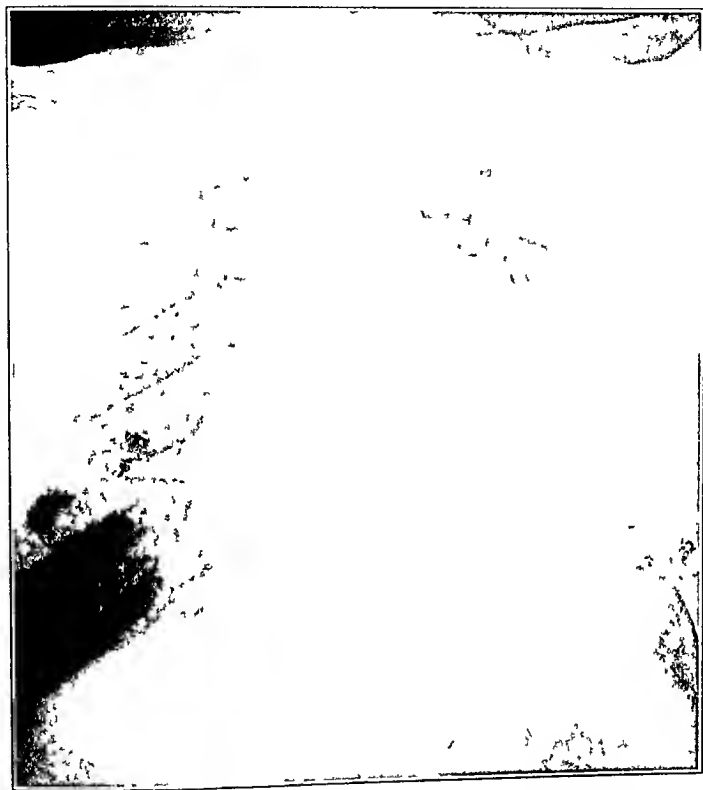


FIGURE 1

was a burning postprandial epigastric pain. He was admitted to another hospital, where a diagnosis of chronic gastritis, acute cardiac decompensation and miliary tuberculosis was made. A roentgenogram taken on April 20, 1938 (Fig 1), showed scattered mottled infiltration throughout both lung fields and thickening of the interlobar septum on the right. The lower two thirds of the left lung was obscured by an enormous cardiac shadow extending from the left axilla to a point 5 cm beyond the right pulmonary hilus. The patient was discharged after 3 weeks.

The patient returned to the hospital 7 months later. A roentgenogram on December 9 showed a marked decrease in the size of the cardiac shadow, which was then normal. The right lung showed no change. On the left there was a pleural reaction casting a haze over the entire lung. The tubercle bacillus was not found.

The patient was not heard from again until June 5, 1939, when he came to the Diagnostic Clinic. His chief

complaint was, as before, a burning pain in the epigastrium. A roentgenogram showed slight clearing of the pleural reaction on the left. He reentered the hospital

July 26. There had been no increase of dyspnea, fatigue, swelling of the ankles, cough or expectoration.

Physical examination revealed a well developed, slightly undernourished, tired looking man. The skin was clear. There were a few small, firm, lymph nodes palpable in the neck and in both axillae. Examination of the ears, eyes, nose and throat revealed no abnormality. The optic fundi were clear. The chest was slightly barrel shaped, and expansion was equal on both sides. The lungs were resonant, and the breath sounds vesicular throughout. At the right base posteriorly there was a faint friction rub. A few posttussive medium rales were heard at the left apex posteriorly and in the first left interspace. The heart was of normal size, with a regular rhythm and no murmurs. There was slight sclerosis of the peripheral arteries. The blood pressure was 130/80. The liver and spleen were not felt. The remainder of the examination was negative. Fluoroscopy revealed normal excursion of the diaphragm on each side. The heart was of normal size and contour.

The cardiac outline was indistinct, with a regular beat of fair quality. A roentgenogram of the chest, taken on July 27 (Fig. 2), showed no change.

The red-cell count was 3,900,000, and the hemoglobin

A diagnosis of chronic miliary tuberculosis was made and the patient was discharged, to be followed in the Outpatient Department. At periodic check-ups he complained of abdominal cramps, occasional diarrhea, cough

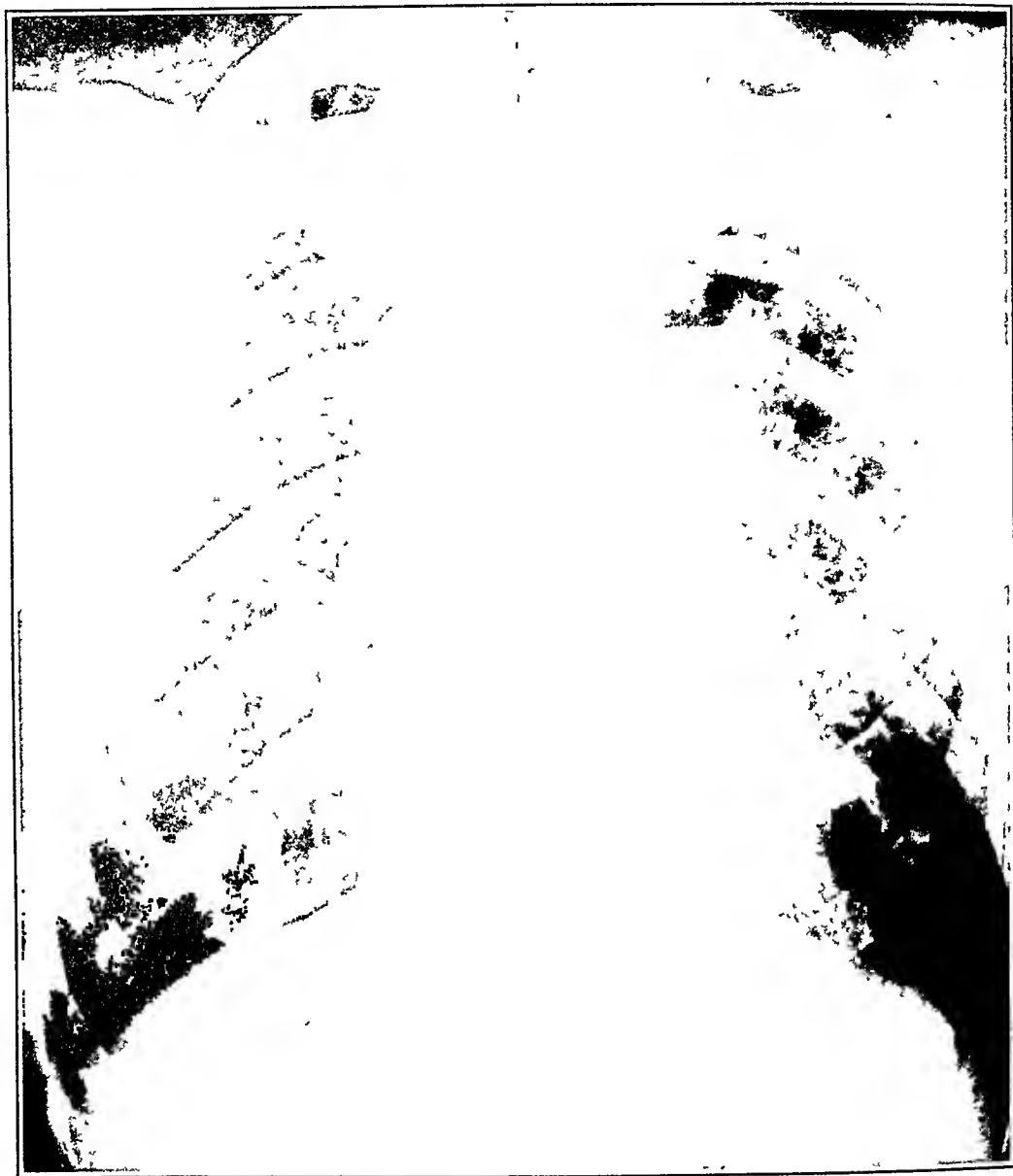


FIGURE 2.

70 per cent (Sahli). The urine was negative, and there was no blood in the stool.

The patient remained in the hospital for 102 days. The temperature, pulse and respirations remained normal. He raised about 30 cc. of semithick, nonodorous, yellowish sputum daily, which was negative for fungi, and for tubercle bacilli even after inoculation of a guinea pig. He was treated by rest, a bland diet and Sippy powders, with relief of his pain, improvement in his general condition and a weight gain of 5 pounds. A subsequent red-cell count was normal. Fluoroscopy of the gastrointestinal tract after a barium meal and a plain film of the abdomen revealed no abnormality. X-ray films of the hands showed no evidence of Boeck's disease. The tuberculin test was positive. A roentgenogram of the chest in the following October showed no change.

and expectoration. His general condition appeared unchanged, as did the roentgenograms of the chest, through September, 1941. The sputum remained negative for tubercle bacilli.

The patient was readmitted May 4, 1942, because of recent slight hemoptysis. Some edema of the lower extremities of a few weeks' duration was present. He had been taking digitalis for 5 months. Physical examination revealed fair nutrition, slight cyanosis of the lips and nail beds and frequent coughing productive of small amounts of yellowish sputum. No lymph nodes were palpable. The trachea was in the midline. There was slight dullness over the right side of the chest but no rales. On the left there was similar dullness, but coarse moist rales were heard over the upper half. The heart did not appear to be enlarged, and was regular except for occa

sional extra beats; no murmurs were audible. The pulse was 80, the respirations 20, and the blood pressure 140/70. There was no orthopnea. The liver and spleen were not palpable. There was slight edema of the extremities.

Repeated sputum specimens were positive for tubercle bacilli on direct smear. The tuberculin test was positive. The red-cell count was 4,200,000, with 90 per cent hemoglobin (Sahli), and the white-cell count was 8500, with a normal differential count. A blood Hinton test was negative. The urine was normal. A roentgenogram showed cavitation of the upper half of the left lung. The distribution of the military lesions seen previously remained unchanged, with some increase in the reaction around the lesions on the left. The cardiac silhouette remained unchanged.

At present the patient is on bed rest. Fever was present up to 100.0°F. during the first 2 weeks after discharge, since when it has been normal except for an occasional rise to 99.0°F.

Although it is appreciated that the recovery of tubercle bacilli from the sputum of this patient does not prove the diagnosis of chronic military tuberculosis, the clinical course of the disease makes such a diagnosis extremely likely.

SUMMARY

A probable case of chronic military tuberculosis is presented, with a review of the outstanding features of this disease.

371 Commonwealth Avenue

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MEDICAL PROGRESS

THE SULFONAMIDES*

II. Their Clinical Use

CHARLES A. JANEWAY, M.D.†

BOSTON

IN the first section of this report¹ the basic knowledge about the sulfonamides was reviewed. It was pointed out that their activity depends on an inhibition of the multiplication of virulent bacteria in the tissues, and that this bacteriostatic activity can be nullified specifically by para-aminobenzoic acid in vitro and by pus and necrotic tissue in vivo. The essential facts about the pharmacology of this group of drugs were presented. With this material as a basis, the second section will be devoted to the use of the sulfonamide drugs in clinical practice.†

In order to make this presentation as useful as possible, I have organized it in the form of answers to a series of questions which constantly occur in the practice of medicine. These answers may seem too dogmatic to some, too general to others. They are far from perfect, but represent the principles worked out from clinical experience and from discussions with others interested in the field. Without committing any of my colleagues to agreeing

with me, I should like to admit my debt to the following, from whose ideas and criticisms most of these principles have evolved: Dr. Paul B. Beeson, Dr. John Dingle, Dr. Maxwell Finland, Dr. Chester S. Keefer, Dr. Perrin Long, Dr. Champ Lyons, Dr. J. A. V. Davies and Dr. W. B. Wood, Jr.

I. What are the indications and contraindications for the use of the sulfonamides?

Because of the brilliant therapeutic results achieved with these drugs, there has been an increasing tendency on the part of physicians to administer them to any patient with a fever. If they were harmless drugs, this would merely be intellectually indefensible, but since they are not only powerful but potentially dangerous remedies, it is as wrong to give them without specific indications as it is to deprive a patient of their benefits when he is seriously ill.

INDICATIONS

Adequate Therapy

Infections due to susceptible organisms should be treated with sulfonamides only if they are severe or spreading, because it is only under these circumstances that these drugs are very effective. Thus, a physician should know the etiology of common infections and possess sufficient clinical judgment to realize when an infection is spread-

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*From the Medical Clinic, Peter Bent Brigham Hospital, and the Department of Medicine and the Department of Bacteriology and Immunology, Harvard Medical School.

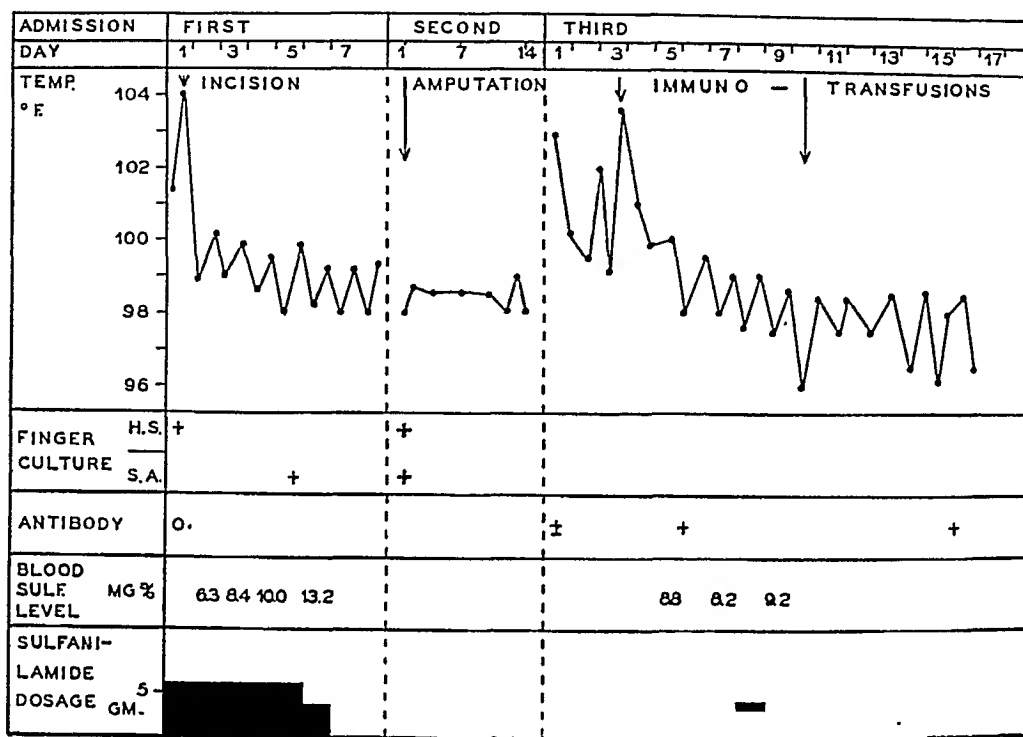
†Assistant professor of pediatrics, Harvard Medical School; visiting physician, Children's Hospital; associate in medicine, Peter Bent Brigham Hospital.

‡In this presentation, the local application of these drugs will not be considered, since this is a strictly surgical problem in which I am neither experienced nor competent.

ing and menacing his patient. In a review published several years ago, I² tabulated the factors which influence the efficacy of sulfonamide therapy, and these still hold true. The drugs are most effective in combating rapidly spreading infections, when the organisms are growing in a serous type of exudate free of sulfonamide inhibitor and when fever is high, as elevated temperature not only

taken from the finger when another incision was made on the 5th day because of continuing tenderness, showed only *Staphylococcus aureus*. Phagocytosis of the hemolytic streptococcus isolated from the finger by the patient's own defibrinated blood was nil (indicating no antibody). The patient was discharged on the 12th day to continue hot soaks to the finger, which still showed tenderness.

Four days later, on the 16th day of his illness, the patient was readmitted because of increasing pain, swelling



MED. 62966

FIGURE 1. Clinical Course of Case 1.

decreases the rate of multiplication of certain bacteria, but markedly increases the bacteriostatic efficiency of the sulfonamides.³ Furthermore, immunity on the part of the patient greatly enhances the therapeutic response. On the other hand, where there is little fever, and particularly when there is tissue necrosis, the sulfonamides have little effect on the lesion except with a highly susceptible organism such as the gonococcus. The following case illustrates some of these points.

CASE 1 (P.B.B.H. S62639, S62778 and S62966) (Fig. 1). The patient, a surgeon, punctured his finger while operating on a man with a hemolytic streptococcus septicemia. Twelve hours later he developed throbbing pain in the finger and had a shaking chill. On admission, high fever, swelling and tenderness of the finger and lymphangitis extending up to the shoulder were observed. The finger was incised, and a Group A hemolytic streptococcus isolated from the serosanguineous fluid was obtained. On moderate doses of sulfanilamide, heat and rest, there was a prompt fall in temperature. Because of the rapid improvement and the marked anorexia and subjective discomfort experienced from the drug, its administration was discontinued on the 6th day. Cultures

and tenderness of the finger. X-ray films showed osteomyelitis of the 2nd and 5th phalanges. The 5th phalanx and the infected portion of the 2nd phalanx were amputated at operation, when small abscesses were opened on either side of the sheath of the flexor tendon. The pus contained both beta-hemolytic streptococcus and hemolytic *Staph. aureus*. Following operation, the finger healed well, and convalescence was uneventful. Swelling had completely subsided and there was only a small amount of serous drainage at one angle of the healing stump, when the patient was discharged on the 13th postoperative day.

For the next 8 days the patient made satisfactory progress, receiving physiotherapy for the stiffness of the finger and daily dry sterile dressings. Except for a reddish-blue color of the stump and a tendency for it to throb when dependent, the finger seemed to be doing well. On the 9th day after discharge and on the 38th day of illness, following a 40-minute walk in the cold through heavy snow, the patient developed chilly sensations, malaise, headache and lumbar backache. He was admitted for the third time with a temperature of 103°F. and a white-cell count of 16,900. The finger appeared normal on admission, and a tentative diagnosis of grippe was made. However, 36 hours after admission, the white-cell count was still elevated, the finger stump and adjacent areas of the hand became reddened, warm and tender, red streaks

appeared running up the arm to the axilla, and the lymph nodes of the axilla became tender and palpable. Consequently sulfanilamide therapy was instituted, and because the patient's blood only showed a low titer of op

and 3rd admissions. However, the drug, despite adequate levels and early treatment, did not sterilize the local lesion, perhaps because of the accompanying staphylococcal infection and suppuration. The flare up that oc

TABLE 1 Infections Responding to Sulfonamide Therapy

TYPE OF INFECTION	DISEASE OR CAUSATIVE ORGANISM	DOSEAGE	BEST DILET	ACCESSORY THERAPY
Local sepsis with spread (including tissue and wound infections), infections of ear, nose, and throat, osteomyelitis	Hemolytic streptococcus (erysipelas, septic throat and so forth)	Regular*	SD (SA)	Heat rest and immobilization incision and drainage
	<i>Staph aureus</i>	Regular	ST (SD)	Heat rest and immobilization incision and drainage
	Gas bacilli	Regular	ST (SD)	Antitoxin x ray
Pneumonia and early empyema	<i>Pneumococcus</i>	Regular	SD (ST)	Antiserum in very severe cases
	Hemolytic streptococcus	Regular	SD (SA)	
	<i>Staphylococcus</i>	Regular	ST (SD)	
	<i>Friedlander bacillus</i>	Regular	ST (SD)	Antiserum if available
Meningitis (lumbar puncture used only to relieve increased pressure and give information on progress)	<i>Pneumococcus</i>	Regular	SD (SP)	Intravenous rabbit antiserum
	Hemolytic streptococcus	Regular	SD (SA)	
	<i>Meningococcus</i>	Regular	SD (ST)	Intravenous antiserum rarely
	<i>H influenzae</i>	Regular	SD (SP)	Intravenous rabbit antiserum
	<i>Staph aureus</i>	Regular	ST (SD)	
Sepsicemia	Most organisms	Regular	SD	For all cases transfusions specific antiserum when available surgical removal of foci
	<i>Staph aureus</i>	Regular	ST	
	Gram negative enteric bacilli	Regular	ST (SD)	
Venereal infections	Gonorrhea	2 gm daily for 10 days	ST (SD)	Fever therapy in resistant cases
	Gonococcal arthritis	6 gm daily	ST (SD)	Aspirin
	Lymphogranuloma venereum	Regular	ST (SD)	
	Chancroid (Ducrey bacillus)	Regular	ST (SD)	
Urinary infections	All organisms except enterococcus	2-4 gm daily unless septicemia present	ST (SD)	Surgery for calculi obstruction and so forth
Miscellaneous infections	Actinomycosis	4 gm daily for many months	SD (SA)	Refr surgery
	Trachoma	Small	SP (SA)	Local treatment
	Brucellosis	Regular	ST (SA)	Chemotherapy for acute attack (trial)
	Anthrax	Regular	ST (SP)	Antiserum
Psittacosis	Various organisms	Regular	SD (SA)	Surgery plasma
Postperal sepsis	Hemolytic streptococcus	Regular	SD (SA)	Transfusions
	<i>Cl welchii</i>	Regular	SD (ST)	Antitoxin
	Mixed infection	Regular	SD (ST)	
Bacterial endocarditis	<i>Str viridans</i> (salivary)	Regular or extra heavy	ST (SD)	Fever therapy neoplasmanne
	<i>Gonococcus</i> or <i>meningococcus</i>	Regular or extra heavy	SD (ST)	Fever therapy

*Regular dosage = sufficient to maintain adequate level

SA = sulfanilamide SD = sulfadiazine ST = sulfathiazole SP = sulfapyridine

sonins for the strain of hemolytic streptococcus from his finger, he was given 500 cc of blood from a donor found to possess opsonins for this strain. With the combination of these measures and local heat and immobilization, the fever, lymphangitis and lymphadenitis subsided rapidly. He was given full doses of sulfanilamide for 3 days, then gradually decreasing doses, because of an adequate blood level (the fluid intake was poor) for the next 9 days. Following a second immunotransfusion, chemotherapy was discontinued and the patient had no further difficulties, except for some circulatory disturbances in the finger and a moderate anemia, which gradually disappeared.

Comment. This case demonstrates the efficacy of sulfanilamide in controlling the acute invasive manifestations of hemolytic streptococcus infection, as shown by the rapid subsidence of fever and lymphangitis on the 1st

curated at the 3rd admission probably had its origin in a thrombophlebitis of one of the veins in the finger stump. Because the patient had had recurrences and did not tolerate sulfanilamide well, he was given antibody by transfusion from two donors whose blood contained opsonins for his organisms. Chemotherapy was then discontinued without further flare up, but this might have occurred anyway. One must not underestimate the value of the time honored surgical procedures of local heat and immobilization in the control of the lymphangitis, nor of amputation in removing the suppurating focus once localization occurred.

It cannot be emphasized too strongly that the effectiveness of sulfonamide therapy will always be limited to a considerable extent by the accuracy of

the bacteriological diagnosis. The treatment of serious infections is difficult when no such diagnosis has been made and when there is no bacteriological check on the progress of the patient. For that reason, before chemotherapy is instituted, cultures of the local lesion and the blood should be taken if possible, as has been customary with lobar-pneumonia patients before the institution of serum therapy. On the other hand, chemotherapy should never be deferred when it is clearly indicated solely because of a lack of laboratory facilities. Table 1 presents in compact form the types of infection in which the sulfonamides are known to be effective, the type of dosage required, the drug of choice and any accessory therapy that should be given.

There are a few infections which are relatively mild, but which menace the community by their infectiousness or the individual by their tendency to produce serious chronic disability. If such an infection is susceptible to sulfonamide therapy, these drugs are certainly indicated in order to prevent serious end results. In this group belong gonorrhea, trachoma, lymphogranuloma venereum and the majority of urinary-tract infections (Table 1). These are usually mild in their early phases, but potentially serious, and all respond to some degree to chemotherapy.

Three-day Trial of Therapy

If a patient is obviously seriously ill with an infectious disease and the physician cannot make a definite diagnosis, he has no right to withhold sulfonamide therapy. The treatment carries a risk of perhaps 0.2 per cent mortality in competent hands, which is too small to justify the denial of a form of therapy that has wide application to many types of infection, provided the patient is seriously ill. Under such circumstances a three-day trial of the sulfonamides is entirely justified. At the end of this period, a bacteriologic diagnosis may have been made, so that the physician will have some basis for a decision about further chemotherapy. If no response to adequate therapy occurs in three days, there is little sense in continuing a drug that has not influenced the course of the disease.

This situation arises most frequently in cases of puerperal infection. The mortality rate of puerperal sepsis due to hemolytic streptococci used to be about 25 per cent. With the prompt administration of the sulfonamides it has been brought to a very low figure. Every hour's delay in starting treatment seriously decreases the patient's chance of survival, and therefore sulfonamides should be administered as soon as a definite postpartum temperature rise above 101°F. occurs. At the same time cultures of the blood and uterine cavity should be taken. However, the vast majority of cases of

puerperal sepsis are not caused by beta-hemolytic streptococci, but by organisms normally present in or near the genital tract, particularly colon bacilli and anaerobic streptococci. The latter do not respond to the sulfonamides; hence in most cases, after a three-day trial, fever and chills may still be present. By this time cultures should be available. If no organisms such as beta-hemolytic streptococci, virulent staphylococci or *Clostridium welchii* have been found, and adequate chemotherapy has not caused a marked reduction in temperature, it should be discontinued.

Prophylactic Therapy

Animal experimentation has demonstrated that the sulfonamides are frequently even more effective in the prevention of infection than in its cure. For this reason their use as prophylactic agents has frequently been advocated. This is a difficult subject on which to make rules, as the decision usually has to be made in the individual case. It is certain that if enough patients receive the sulfonamides prophylactically, someone is going to die from them. Thus, there is a definite though probably minute risk to life. That this really exists is attested by the death recently reported by Stowell and Button.⁴ Beyond this there is the risk of sensitizing the patient, so that future sulfonamide therapy for more important reasons may produce severe reactions. Against these risks should be balanced the chances of infection and the dangers therefrom. The following are situations in which these drugs should probably be used prophylactically. In general, the prophylactic dose is smaller than the therapeutic dose.

Definite indications include the following: dirty, traumatic wounds; burns; influenza, during an epidemic when complicating bacterial pneumonia is frequently observed; known exposure to gonorrhea; cases of rheumatic or congenital heart disease for twenty-four hours before and seventy-two hours following dental extraction, tonsillectomy or any operative procedure that might permit the entrance of bacteria into the blood stream (in the hope of preventing bacterial endocarditis); and contamination of the peritoneal or pleural cavities.

Questionable indications include the following: the prevention of scarlet fever or hemolytic streptococcus infection in a person with known exposure, for whom the disease would constitute a serious hazard; under certain conditions, as a prophylactic against the activation of rheumatic fever by preventing hemolytic streptococcus infection of the pharynx (the use of the drug under these circumstances must be decided on the merits of the individual case; such prolonged administration as is necessary for good effects may be harm-

ful per se and certainly is not without risk⁴; more evidence is needed on this score⁵); and inlying catheter, that is, patients on constant bladder drainage (this practice is justifiable for a period of a week or so).

CONTRAINDICATIONS

Infections Not Responding to Sulfonamides

Such infections exist, and constitute an important contraindication to the use of these drugs, when a definite diagnosis can be made. When it is known that the therapy will do no good, will only serve to make the patient more uncomfortable, and may complicate his illness, the doctor should have sufficient courage to avoid giving it, even though the family may want to know why the patient is not receiving a sulfonamide drug. Certain diseases in which these drugs have no favorable effect are as follows: "virus" or atypical pneumonia and psittacosis; influenza, in the absence of secondary bacterial infection; common cold; typhoid fever; typhus and Rocky Mountain spotted fever; infections due to neurotropic viruses (poliomyelitis and encephalitis); acute exanthemata in the absence of bacterial infection; infectious mononucleosis, in the absence of secondary infection; puerperal infections due to anaerobic streptococci; urinary-tract infections due to enterococci; toxic manifestations of scarlet fever; diphtheria; and tetanus. In certain other diseases, such as tularemia and brucellosis, the evidence that the sulfonamides do more than produce temporary improvement is scanty, but they probably deserve a trial for several days.

Mild Illness or Localized Infection

One of the truths which was apparent to former physicians who had few specific remedies was that most patients got well if let alone and given a reasonable chance. This simple fact seems to have been forgotten, and there is a growing tendency to replace the therapeutic nihilism of former years with therapeutic overenthusiasm, aided and abetted by the glowing reports of new remedies to be found in popular magazines and the attractive brochures that arrive by the score in each week's mail.

The sulfonamides are not very effective, particularly against organisms like the hemolytic streptococcus, when there is no fever and the inflammatory process is indolent. Thus, attempts to rid the throat of hemolytic streptococci in the absence of symptoms or to treat a mild attack of acute tonsillitis with one of the sulfonamides are usually doomed to failure. The evaluation of treatment in tonsillitis requires great judgment. Although studies have indicated that the sulfonamides have little

effect on the disease,⁶ some observers feel quite confident that its severe complications can be reduced in frequency and successfully combated by chemotherapy. I rarely use the sulfonamides unless the temperature exceeds 102°F. or there is evidence of extension of the infection, such as sinusitis, adenitis or otitis media. On the other hand, in cases of acute nephritis, sulfanilamide has been recommended as a means of diminishing focal streptococcal infection, particularly in the tonsils.⁷ Its main virtue is to reduce the number of bacteria and to make possible the early extirpation of the focus without producing a flare-up. In such cases it should only be used under very close supervision.

Localized infection, associated with the accumulation of pus, is resistant to sulfonamides, because of the inhibitor present in the pus. The drugs are very effective in aiding the localization of spreading infections, but once localization takes place they may have little effect in actually getting rid of bacteria. Thus, in puerperal sepsis, hemolytic streptococci are usually found in the lochia long after sulfonamides have cured the disease. If all the pus can be removed from an abscess, such as an empyema cavity, the sulfonamides may then assist cure without resort to surgery,⁸ but the total removal of pus is often technically impossible by aspiration. A three-day course of chemotherapy starting twelve hours before incision of a severe purulent infection such as a carbuncle, may occasionally be worthwhile in an attempt to prevent metastatic infection from the trauma of operation.

Previous Severe Toxic Reactions to Sulfonamides

These drugs are now being used so extensively that a physician should always ask the patient whether he has had them before starting therapy, and if so, how he tolerated them. If he had a severe reaction, the physician should use a different sulfonamide and proceed with some caution. I believe that intensive chemotherapy with a different sulfonamide drug should be used if the patient is desperately ill. If, however, treatment can be deferred for a short time, he should be given a test dose of 0.5 gm. of the drug. If no untoward symptoms appear in twelve hours, full doses can probably be safely used. Even if a patient has had no reaction to a previous course of sulfonamide therapy, particularly a short one, the physician should be on the alert for toxic reactions during a second course. I recall a patient who developed high fever within twelve hours of the start of a course of sulfathiazole for a urinary tract infection. On careful inquiry it was found that she had received sulfathiazole six months previously. This course had produced sterilization, but since it lasted only four days,

all the drug was excreted before she became sensitive, and hence no reaction occurred at that time. Sensitivity persisted, however, and she developed an accelerated reaction when the drug was readministered six months later.

Acute Rheumatic Fever

Patients with this disease actually become sicker when sulfonamides are given.^{9, 10} The drugs may also be dangerous in certain cases of acute disseminated lupus erythematosus.^{11*}

Leukopenia

At this point, it is worth emphasizing that leukopenia or agranulocytosis is *not* a contraindication to sulfonamide therapy in cases of severe pyogenic infection. In overwhelming pneumococcal, hemolytic streptococcus or staphylococcal infections, the white-cell count may be depressed to levels of less than 1000, with almost complete absence of polymorphonuclear leukocytes. Whenever a physician meets this situation, he should bear in mind the possibility of leukemia. However, this depression of the bone marrow can occur in severe infection. From the standpoint of therapy it is an indication for immediate, intensive chemotherapy, since it is a grave prognostic sign. The circulars on pneumonia therapy issued by the Massachusetts Department of Public Health in years past have stated that leukopenia is an indication for serum therapy and a contraindication to chemotherapy. This, I believe, is entirely wrong. Serum therapy acts only by making possible phagocytosis of pneumococci by leukocytes in the lung and by the reticuloendothelial cells lining the vascular system. The number of circulating polymorphonuclear leukocytes is no indication of their number in the lung lesion, where their action on the pneumococci must take place, but presumably there will be fewer at the spreading margin of the lesion if there are very few in the peripheral blood. Therefore serum therapy is apt to be less effective in such cases. On the other hand, chemotherapy, which attacks the organisms themselves and can destroy pneumococci without the intervention of white blood cells in the pneumonic lung,¹² is the most effective form of treatment, since it stops the multiplication of the organisms, which is responsible for the bone-marrow depression. In such severe cases of pneumonia, combined therapy is probably most effective, so that once intensive chemotherapy is under way, serum should also be used. This of course applies to leukopenia before chemotherapy begins. Leukopenia appearing after chemotherapy has been instituted, when the patient is improving, is usually due to the drug itself.

*Although sulfonamides should not be given for the treatment of rheumatic fever itself, they should not be withheld from rheumatic patients when there is a clear indication, such as septicemia or pneumococcal pneumonia.

II. Which sulfonamide drug should be used?

There are several factors to be weighed in the choice of a sulfonamide drug for the treatment of any particular case. These are the relative efficiency of the different drugs in the particular infection; the previous experience of the patient with sulfonamides; and pharmacological considerations.

The relative efficiency of the different drugs in different types of infection is partially covered by Table 1. In general, sulfanilamide is less potent than the other sulfonamides, except perhaps against Group A hemolytic streptococci, so that it should be used only in infections due to the latter organism or where its high diffusibility and lack of toxicity for the kidney are assets that outweigh its drawbacks. Sulfanilamide is ineffective in pneumonia, and gives comparatively poor results in gonorrhea. There are few bacteriologic reasons for selecting one of the three substituted sulfonamides over the others, except in the case of infections due to staphylococci, Clostridia or gram-negative enteric bacilli, where sulfathiazole seems to have a slight advantage. In general, sulfathiazole and sulfadiazine possess somewhat greater potency than sulfapyridine.

The previous experience of the patient is important, and if he has had toxic reaction to a given drug, the physician should use a different one. This is one of the best reasons for having three different substituted sulfonamide drugs available.

Pharmacological considerations weigh most heavily in the choice of a drug. Neither sulfanilamide nor sulfapyridine should be used routinely, because of the subjective discomfort they produce in the patient, either malaise, headache and anorexia or nausea and vomiting. Sulfathiazole and sulfadiazine are much better tolerated. However, sulfanilamide is recommended in the treatment of acute hemorrhagic nephritis because it rarely injures the kidney. It is useful also for subcutaneous or intrathecal administration, and may be employed to initiate chemotherapy in meningitis because it enters the spinal fluid so readily.

In general, sulfadiazine is the drug of choice in the systemic chemotherapy of all types of infection, with the following possible exceptions:

Urinary tract. Sulfathiazole is potent in small doses against the common organisms causing this type of infection. It is rapidly excreted in the urine in high concentrations and hence gives best results on the smallest dosage.

Gonorrhea. In this disease, sulfathiazole and sulfadiazine give equally good results. It seems worth while, however, to use sulfathiazole and to save sulfadiazine for more serious infections,

when its lack of side effects may be very helpful, because large doses must be given.

Staphylococcal infections. Sulfathiazole is probably the most potent drug (except penicillin,¹³ which unfortunately is not yet generally available) against this stubborn and dangerous organism.

Gas gangrene. Sulfathiazole has a wider range of effectiveness against Clostridia, particularly *Cl. septicum*, than the other sulfonamides.

Anthrax. Sulfathiazole and sulfapyridine are reported as better than the other sulfonamides.¹⁴

In the treatment of meningitis, much has been made of the fact that one drug traverses the blood-brain barrier more readily than another. Sulfathiazole is always present in the spinal fluid in much lower relative concentration than any of the other drugs, whereas the concentration of sulfadiazine in the thecal space rises slowly. For this reason sulfapyridine has been recommended for the treatment of pneumococcal meningitis, and sulfanilamide for hemolytic streptococcus meningitis, since both drugs enter the spinal fluid rapidly. However, success in the treatment of meningitis with sulfathiazole suggests that the concentration of drug in the spinal fluid may not be important except in so far as it reflects its concentration in the tissue spaces. Because treatment in meningitis must frequently be continued for more than ten days, sulfadiazine is probably best, except in staphylococcal infections.

When parenteral administration is used, pharmacological considerations are all-important. For intravenous use, sodium sulfadiazine has great advantages over the sodium salts of sulfathiazole or sulfapyridine. It is excreted much more slowly, so that a patient may be treated by an initial large dose followed by injections of 2 gm. every eight to twelve hours with the maintenance of an effective blood concentration. The rapid excretion of sodium sulfathiazole makes it almost impossible to maintain a satisfactory blood level without producing renal damage, and the same is true to a lesser degree of sodium sulfapyridine. Although both these drugs may be given safely once, repeated doses are dangerous. For subcutaneous administration either 0.5 per cent solutions of the sodium salts of sulfadiazine,* sulfathiazole or sulfapyridine in physiologic saline solution, or else 0.8 per cent sulfanilamide in saline, may be used. The latter is preferable where it is efficacious, since it is rapidly absorbed. When dilute solutions of the sodium salts of the other sulfonamides are given subcutaneously, absorption may be slow and lead to sulfiding up in the blood after repeated doses.

*Sodium sulfadiazine may be used in concentrations as high as 2 per cent subcutaneously.

For intrathecal use, only 0.8 per cent sulfanilamide should be used, because solutions of the sodium salts are too alkaline; it is doubtful, however, whether intrathecal injection is ever necessary.

III. What is the dose, and how shall it be given?

As has been previously stated, the blood concentration depends on the balance between the rate at which the drug is entering the circulation, usually from the bowel, and the rate at which it is being cleared in the urine. A large initial dose is given, so that the blood level rises rapidly to an effective concentration, and from then on doses are given so as to maintain that concentration by balancing the amount excreted by the kidney. The rate of clearance by the kidney depends on the functional capacity of that organ. The physician should always try to assess renal function by questioning the patient about nocturia and previous nephritis and by examining the urine.

In the presence of normal renal function, the excretion of sulfanilamide is hastened by an increase in the urinary output. With the other sulfonamides, the rate of excretion of the drug is influenced to a much lesser extent by the urinary output. Therefore, when giving sulfanilamide the fluid intake is usually restricted to 2500-3000 cc., whereas with the other drugs fluids are forced, to prevent concentration of the urine and precipitation of the free or conjugated drug in the kidney.

One of the commonest errors is too small dosage. A little sulfonamide treatment is worse than none, because it either has no effect or partially suppresses the infection, whereas the organism has a chance to develop some degree of sulfonamide resistance. It prolongs the period of chemotherapy and thus increases the chances of serious toxic reactions. Once the decision to use chemotherapy is made, the physician should try to get the infection under control as rapidly as possible.

The route of administration should always be oral if possible. This assures slow, steady absorption, and hence a more constant blood level. In patients who are unable to swallow the tablets, they should be pulverized and suspended in a little water, milk or fruit juice. In comatose patients—those with meningitis, for example—a nasal tube can be introduced into the stomach and a suspension of the drug in water given through it.

Parenteral administration is indicated under the following conditions:

For the initial dose in patients with very severe infections. Frequently patients who are very ill are distended, and often nauseated. By giving the initial dose intravenously, an adequate blood level is immediately established, and several hours

are saved, which may be vitally important in bringing the infection under control.* Oral administration of the subsequent doses, if possible, assures continuous absorption and maintenance of an effective level.

In patients who are unable to take oral therapy because of vomiting or for surgical reasons. Ab-

levels following injection, and close attention must be paid to the fluid intake and urinary output.

Table 2 gives the recommendations for dosage in convenient form for reference. The doses given are for an average 150-pound adult. The dosage for children and larger or smaller patients should be adjusted according to weight. In small children,

TABLE 2. Dosage Schedules for Average 150-Pound Adult.

DRUG*	INITIAL DOSE	MAINTENANCE DOSAGE	DESIRED BLOOD LEVEL	FLUID INTAKE	DESIRED URINARY OUTPUT	DOSAGE OF SODIUM BICARBONATE
	gm.†	gm.	mg./100 cc.		cc./24 hr.	
ORAL ADMINISTRATION						
REGULAR DOSAGE FOR GENERAL INFECTIONS						
S.A.	4.0	1-1.5 every 4 hr.	8-15	Restrict	1500	Equal amounts
S.P.	4.0	1 every 4 hr.	5-10	Force	2000	None
S.T.	5.0	1-1.5 every 4 hr.	3-5	Force	2000	None
S.D.	5.0	1.5 every 6 hr.	8-15	Force	2000	None
GONORRHEA, UNLESS SEPTIC COMPLICATIONS EXIST						
S.T.	3.0 (first 24 hr.)	0.5 4 i.d.	—	—	1500	None
S.D.	3.0 (first 24 hr.)	0.5 4 i.d.	—	—	1500	None
URINARY-TRACT INFECTIONS, UNLESS VERY SEVERE						
S.T.	—	0.5 4 i.d.	—	Force	2000	May be used to keep urine alkaline (both drugs more effective in alkaline urine)
S.D.	—	1.0 4 i.d.	—	Force	2000	
INTESTINAL INFECTIONS AND PREOPERATIVE REDUCTION OF BACTERIAL FLORA OF COLON						
Sulfaguanidine	6.0‡	3.0 every 4 hr.	<2			
Sulfasuxidine	5.0‡	2.5 every 4 hr.	<2			
INTRAVENOUS ADMINISTRATION						
S.A.	Not used					
Sod. S.P.	4.0	Shift to oral				
Sod. S.T.	4.0	Shift to oral				
Sod. S.D.	5.0	2.0 every 8-12 hr.	8-15	Force	2000	None
SUBCUTANEOUS ADMINISTRATION						
S.A. (0.8%)	4.0	3.0 every 8 hr.	8-15	Moderate	1500	
Sod. S.D. (0.5-2%)	5.0	2.0 every 8 hr.	8-15	Force	2000	

*S.A. = sulfanilamide; S.D. = sulfadiazine; S.T. = sulfathiazole; S.P. = sulfapyridine.

†For conversion to grains, 1 gm. = 15 gr.

‡Initial large dose probably only necessary in dysentery when diarrhea is present; in absence of diarrhea, dose of 0.25-0.3 gm. per kilogram of body weight may be given daily in three or four divided doses (every 6 or 8 hr.).

sorption of these drugs is best in the stomach, so that their administration through a Miller-Abbott tube into the duodenum or jejunum may not be a very reliable method unless carefully controlled by determinations of the blood level. Hence, in severe peritonitis, it is probably best to use parenteral administration.

In patients in whom it is difficult to establish blood levels. In such patients, intravenous doses may be used to supplement oral therapy (Case 2).

It must be emphasized that prolonged intravenous injection of the sodium salts of the substituted sulfonamide drugs carries a high risk of renal complications because of the massive excretion of the drug resulting from the high blood

somewhat larger doses in proportion to body weight are used.

In patients with diminished renal function, the clearance of sulfonamides roughly parallels urea clearance. To establish an adequate level, the initial dose is only reduced to about 80 per cent of the usual one, but subsequent maintenance doses are reduced in proportion to the reduction in renal function, because of the delay in excretion. In such patients, whenever possible, the blood level should be determined frequently, and where facilities are not available, dosage should be reduced as soon as there is a satisfactory therapeutic response.

Very little has been said above concerning the use of the two sulfonamides that have been recommended for strictly intraintestinal chemotherapy, namely, sulfaguanidine¹⁵ and succinyl sulfathiazole or sulfasuxidine.¹⁶ The former is not absorbed to any great extent, but is quite soluble.

*This is very important (Case 6). Enough individuals absorb these drugs irregularly when given by mouth (Case 2) to make it risky to depend on the oral route when starting therapy in a very sick patient.

The latter is probably hydrolyzed in the bowel to sulfathiazole, which is the most potent of the sulfonamide drugs against the coliform organisms and the Clostridia, which make up a large portion of the bacterial flora of the colon. In the lower intestine sulfathiazole is very little absorbed, hence it is largely excluded from the blood. Toxic reactions are apparently more frequent with sulfaguanidine than with sulfasuxidine, perhaps because the former is more readily absorbed. Both drugs are effective in the treatment of bacillary dysentery and of dysentery carriers, and are also effective, when given for about five days preoperatively, in effecting a marked reduction in the bacterial flora of the stools, thereby reducing the likelihood of infection in surgery of the large bowel. In ulcerative colitis, sulfaguanidine has failed to produce much effect, and sulfasuxidine is still on trial. Dosage of either drug should be large, in an effort to saturate the bowel with the drug in solution, which will then be effective wherever it comes in contact with the mucosa. With diarrhea, more frequent and larger doses must be used. If a loop is excluded as with colostomy, the drug must be introduced into the distal loop in order to affect its contents. Prolonged use of either drug should be avoided, since certain essential growth factors, such as biotin, are synthesized to a considerable extent by the bacteria of the bowel.¹⁷

IV. When should the blood level be determined?

The determination of sulfonamide concentrations in the blood and other body fluids has been of enormous value in putting sulfonamide therapy on a rational basis. However, enough is now known of the pharmacology of these drugs to make the determination of blood concentrations superfluous in many cases. When the patient responds promptly to treatment and has no abnormality of renal function, there is no need for determining the blood level. On the other hand, there are some situations in which it should be determined. These are as follows: when a patient does not respond to therapy in twenty-four to thirty-six hours; when a patient has an abnormality of the urinary tract—diminished renal function or incontinence—so that the output cannot be measured; and when parenteral therapy or administration through a stomach or duodenal tube must be used.

V. How long should therapy be continued?

This question is difficult to answer in general terms. It depends on two factors: the rate of elimination of the drug (dependent on the properties of the drug and the renal function) and the properties of the infecting organism. In general, therapy

should be continued until all evidence of infection has disappeared for at least forty-eight hours; in the case of pyogenic infections, until localization has occurred and adequate drainage has been established; or, in certain cases, until sufficient antibody has been developed or administered to the patient to maintain a cure.

Bacterial infections differ in the manner in which recovery takes place. In pneumococcal pneumonia, spontaneous cure is effected by crisis or by lysis, owing to the development of both local and humoral immunity as the result of infection. Administration of serum in sufficient doses will produce an artificial crisis as soon as sufficient antibody is present.¹⁸ The effective sulfonamides likewise produce either a critical or a gradual fall in temperature. This is because pneumococci are readily destroyed, either by phagocytosis if sufficient antibody is present¹⁹ or by autolysis if their growth is inhibited by the sulfonamides.¹² Therefore, once the temperature has become normal, usually forty-eight hours will suffice completely to eradicate the infection, and the drug may be discontinued at the end of this period. On the other hand, hemolytic streptococci are much harder to destroy, and therapy must be continued longer after the temperature has become normal if relapse is to be prevented. In the case of erysipelas or cellulitis, evidences of local infection, such as local redness and edema, may persist after the temperature becomes normal, and chemotherapy should be continued until these disappear. In cases of deep infection, such as mastoiditis and osteomyelitis, it may be impossible to detect evidence of continued infection by any method, and the decision of when to stop the administration of the sulfonamides is very difficult. Such aids as x-ray examination and determination of the sedimentation rate must be used, and therapy should be continued for about two weeks after apparent cure.

Staphylococcal infections are notoriously resistant to all forms of therapy. In such cases, chemotherapy can only be an adjunct, which aids in the localization of the infection and in the clearing of the blood of organisms, and which helps to prevent the development of new foci, particularly in the kidney. Sulfathiazole should be used until adequate localization occurs, the blood is sterile and the focus is draining either spontaneously or as the result of surgical intervention. In meningitis, temperature is a notoriously poor index of recovery, and many patients who do recover will run a fever for a week or two after recovery really occurs. The spinal-fluid findings are most reliable. When all polymorphonuclear leukocytes disappear from the spinal fluid, it is probable that the infection

has been overcome, and the dosage may be reduced over a period of several days. If no signs of recurrence appear, the drug is then discontinued (Case 4).

Chronic infections, such as actinomycosis or subacute bacterial endocarditis, necessitate the continuation of chemotherapy for weeks or months, even though a patient may seem well. In acute infections the aim should be to cure the disease in less than ten days if possible, as serious toxic reactions are much less frequent during this period.

VI. What should be done if there is no response to therapy?

If fever continues despite thirty-six hours of adequate chemotherapy, certain possibilities should be immediately checked.

Incorrect diagnosis. This is perhaps the most frequent reason for therapeutic failure. For example, what is taken to be pneumococcal pneumonia may actually be so-called "atypical" or "virus" pneumonia, pulmonary infarction or typhus fever, none of which respond to chemotherapy. Therefore, the diagnosis should always be checked in such cases, particularly with reference to the bacteriology of the case.

Inadequate blood level. The blood level should be determined, or if this is impossible, and there is no other reason for the failure of therapy, the maintenance dose should either be increased or a single supplementary dose of 2 or 3 gm. of sodium sulfadiazine given intravenously to raise the level promptly (Case 2).*

Presence of pus. This should always be suspected when a patient fails to respond to therapy and continues to run fever. The following case illustrates this very clearly.

CASE 2 (P.B.B.H. M61660 and S69469). The patient, an 18-year-old boy, who had had chronic sinusitis for 5 years, was admitted on the 3rd day of an illness characterized by coryza, cough with blood-streaked sputum and pleuritic pain over the right side of the chest. On admission the temperature was 101.2°F., the pulse 110, the respirations 52, and the white-cell count 19,800. Examination of the chest showed signs of fluid or consolidation on the right, and x-ray films revealed patchy consolidation of the right lower lobe with haziness at the base, interpreted as representing bronchopneumonia with pleurisy. A blood culture was sterile, and a Type 19 pneumococcus was isolated from the sputum.

Despite large doses of sulfadiazine, 5 gm. initially and 1.5 gm. every 4 hours (later increased to 2 gm.), the temperature fluctuated between 101.2 and 103.6°F., the white-cell count rose to 39,000, and signs of fluid, both by physical examination and x-ray study, became increasingly

prominent. The chest was tapped on the 4th and 8th days, and after a long delay, growth of Type 19 pneumococcus was obtained. Therefore, the patient was submitted to closed intercostal drainage on the 8th day, rib resection on the 12th day, and again on the 28th day, before the temperature finally subsided and recovery took place. Sulfadiazine was discontinued after the second operation.

Comment. This case illustrates three points particularly: first, the difficulty experienced in achieving satisfactory blood levels on oral therapy alone in occasional cases; second, the necessity for checking blood levels and looking for pus when there is no therapeutic response; and third, the failure of sulfonamide therapy when there is an accumulation of pus. Despite large doses of sulfadiazine by mouth (5 gm. initially and 1.5 gm. every 4 hours), the blood level was only 3.0 mg. per 100 cc. after 24 hours of therapy. Therefore, the dose was increased to 2 gm. every 4 hours, with a rise in the level to 7.0 mg. per 100 cc. Since this was considered too low, and the infection was not yielding to treatment, an additional 2 gm. of sodium sulfadiazine was given by vein. The next day the level was 11 mg. per 100 cc., but fever continued, and on the following day pus was found in the chest.

Drug fever. Frequently the cause of continued fever in a patient receiving sulfonamide therapy is the drug itself. Of all the problems raised by the introduction of these remedies into clinical medicine, the confusion caused by drug fever is most constantly cropping up. There is no way to be certain when fever is due to the drug. However, if it occurs after the patient has apparently been cured, is accompanied by rash, adenopathy and arthralgia, and is characterized by a paucity of symptoms, relative bradycardia and a normal white-cell count, the diagnosis is simple. Unfortunately, both tachycardia and leukocytosis may occur (Case 6).

Drug fever may be associated with chills, which usually come on soon after the tablets are swallowed, delirium, extreme headache and malaise, or may be practically asymptomatic. The fever may be low grade, septic in type, or high and sustained. It usually begins from the fifth to the twelfth day after treatment is started, and is most confusing when it complicates a disease that responds slowly to therapy, such as staphylococcal infection, so that drug fever is superimposed on the fever due to the infection itself. As already mentioned, if a patient has previously had a course of sulfonamide therapy, and has become sensitized, he may develop drug fever within a few hours after receiving the drug a second time.

The best way to present the problem of drug fever is to cite a number of cases that have occurred in my own experience.

CASE 3 (P.B.B.H. S63445) (Fig. 2). This 26-year-old man was admitted for treatment of an acute urethritis and prostatitis of 5 days' duration. Gram-negative intracellular diplococci were present on smear, and the gonococcus was

*In certain patients an unusually large percentage of the circulating sulfonamide is present in the acetylated form. This is not therapeutically active, nor is it measured by the ordinary blood-level determination. In cases of inadequate level, when good-sized doses have been given, it is worth while, if possible, to determine both the free and the total sulfonamide to check on this possibility.

isolated from the prostatic secretion. He was placed on very large doses of sulfanilamide and did very well, with disappearance of the urethral discharge and of gonococci by culture. However, the blood level rose to 16 mg per 100 cc. of sulfanilamide as a result of the large doses,

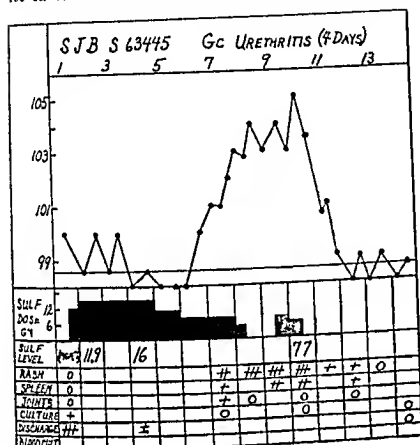


FIGURE 2 Clinical Course of Case 3

and on the 6th and 7th hospital days the temperature rose, reaching 104°F on the 8th day. With this fever, the patient developed transient pains in the metatarsal region of the right foot, a purplish, blotchy rash and a palpable spleen. The drug was stopped temporarily, but because the temperature did not fall, its administration was resumed on the 9th and 10th days. With this the patient had a shaking chill, the temperature rose to 105°F, the rash became more prominent, and the spleen remained palpable. The first diagnosis had been drug fever, but because of failure of the fever to remit on stopping the drug, the physician felt that the patient probably was developing gonococcal septicemia. When the drug was stopped for a second time and large amounts of fluid were given by mouth and by vein, the temperature soon fell to normal and the rash disappeared.

Comment. This is a classic example of severe drug fever, with onset on the 6th day, rash, arthralgia and splenomegaly. The high, flat temperature is quite characteristic of the severe form of intoxication. The chill on readministration of the drug is likewise frequently observed. Nevertheless, the physician in charge of the patient feared that the patient was suffering from an extension of his infection to the blood stream. Since this had occurred in the face of a high blood sulfanilamide level, there would have been no sense in continuing the drug even if the symptoms had thus been correctly interpreted.

CASE 4 (PBBH M61218) This 17-year-old boy was admitted because of drowsiness, headache and vomiting for 24 hours. He was found to have classic signs of meningitis, with a white-cell count of 33,200. A lumbar puncture showed markedly increased pressure and cloudy, yellowish fluid containing 12,500 cells per cubic millimeter, nearly all polymorphonuclears. Culture of the fluid yielded Type 1 meningococci. In the first 24 hours the patient was given 10 gm of sodium sulfadiazine intravenously because of incessant vomiting, which prevented oral therapy. Thereafter he received 1 gm of sulfadiazine by mouth every 4 hours for 3 days. On this regimen the pulse fell from 120 on admission to an average of 60, the temperature from a range of 100–102°F on the 1st day to 99–100°F on the 4th day. Since the blood level was only ranging from 2.7 to 6.6 mg per 100 cc with a spinal fluid level of 7.4 mg per 100 cc, and the patient was complaining of a return of headache the dose was increased to 1.5 gm every 4 hours. Thereafter the level ranged from 10–13 mg per 100 cc, and he made steady improvement. On the 8th day, the dose was reduced to 1 gm every 4 hours, and on the 10th day to 1 gm every 6 hours. The white-cell count remained normal after the first 2 days, and lumbar punctures revealed a steady decrease in the number of cells. On the 3rd day only about 300 per cubic millimeter were present of which 30 per cent were lymphocytes, and cultures were negative. On the 8th day there were 37 cells, all but one of which were lymphocytes, and consequently the dose of sulfadiazine was reduced. From the 9th day on, the patient began to run an afternoon fever of 99°F for 3 days then rising to 100°F, and from the fifteenth to the seventeenth day reaching 101°F. The spinal fluid still showed only a few lymphocytes, but the initial pressure was high (300 mm of water), and the dynamic reactions were rather sluggish. Although it was feared that the patient might be developing a localized focus of infection in the meninges or a partial block because of the increasing fever and lack of symptoms, the drug was discontinued. Within 36 hours the temperature became normal, but the white cell count fell to 4000 and a typical maculopapular rash of the erythema nodosum type developed over the extremities, which disappeared in 4 days.

Comment. This type of low grade septic fever is most confusing. All forms of purulent meningitis are notoriously prone to relapse after sulfonamide therapy, hence the administration of the drug was continued for a long time after all other evidence of infection except fever had disappeared. The prompt subsidence of fever when the drug was discontinued, coupled with the appearance of rash and leukopenia, makes it very likely that the drug was the cause.

CASE 5 (PBBH M58886) (Fig 3) (previously reported by Michael²⁰) This 35-year-old woman developed chills, headache and general malaise with a fever of 101°F 6 days before entry. These symptoms with prostration persisted until 2 days before entry, when she began to feel worse. She developed cough, with the production of large amounts of dark brown sputum, and noticed soreness in her right side. On admission, the temperature was 104°F, the white cell count 10,900, and examination revealed signs of consolidation at the right base. Subsequent bacteriologic studies revealed virulent *Staph aureus* in pure culture in the sputum, and a diagnosis of staphylococcal pneumonia complicating influenza was made. Serologic evidence for recent infection with influenza A virus was obtained from her blood. This type of infection was known to be severe and resistant to therapy, so large doses of sulfathiazole (1.5 gm every 4 hours) were given and a blood level ranging from 6.4 to 9.8 mg per 100 cc was achieved.

Although the temperature tended downward the first 3 days, thereafter it rose gradually, reaching 105°F on the 12th day, with a pulse of 120 and a white cell count of 7100 (24,000 on the 8th day). With this increase in

temperature, the patient appeared sicker, with signs of consolidation involving more of the right lung and the left base as well (confirmed by x-ray study), and continued to cough with production of large amounts of tan-colored, blood-streaked sputum. However, on the 13th day she appeared slightly better, although the temperature was

and 4 gm. of sodium sulfathiazole and 18,000 units of scarlatinal antitoxin were given by vein. In the next 6 hours two more doses of 2 gm. of sodium sulfathiazole were given intravenously, as well as large amounts of 5 per cent glucose in saline, since the patient had not voided for 12 hours. Within 12 hours after starting intravenous

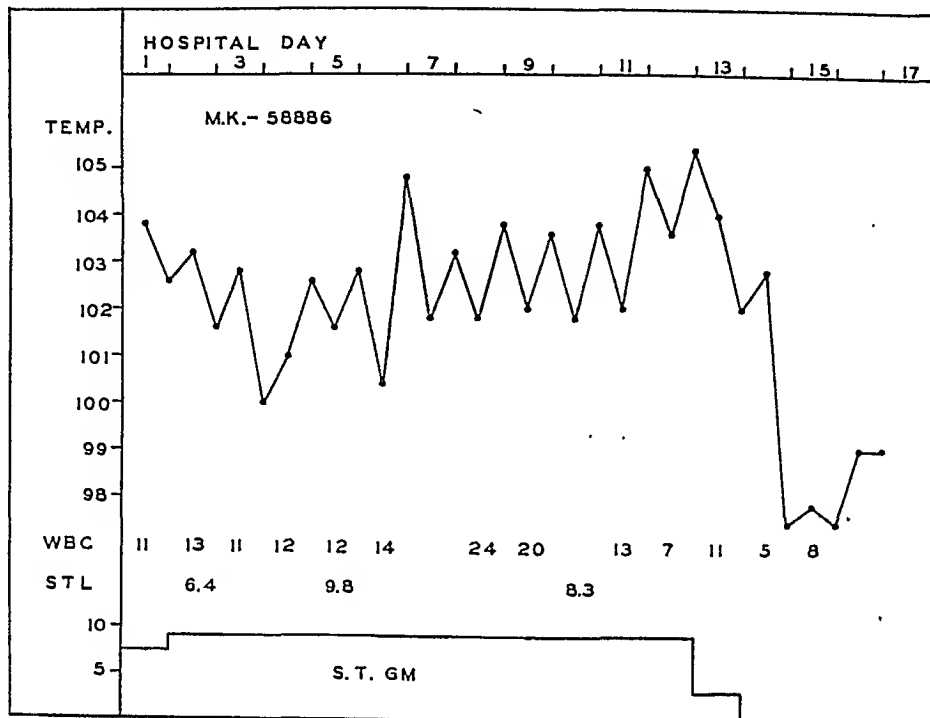


FIGURE 3. *Clinical Course of Case 5 (reproduced by permission of the Journal of the American Medical Association).*

104°F., and in view of the high, sustained fever, the fall in the white-cell count, and the slight improvement of chest signs, it was decided to discontinue sulfathiazole. The next day the temperature fell precipitously to normal, the white-cell count went down to 4600, and the patient began an uneventful convalescence.

Comment. There seems little doubt that severe drug fever was superimposed on a very severe infection. Where one began and the other ended is impossible to determine. It is not at all impossible that fever, due to the drug, with its potentiation of the bacteriostatic action of the sulfonamides, actually aided this patient in recovering from this severe disease. This case illustrates the rapid recovery from toxic reactions to sulfathiazole when the drug is stopped.

CASE 6. The patient, a 30-year-old white woman, had an uneventful term delivery of her second child. Two days post partum she developed abdominal cramps, anorexia and a fever, which rose rapidly to 105.8°F. with a pulse of 160. The white-cell count was 18,000. She was given 1 gm. of sulfadiazine followed by 2 gm. in 4 hours, and 1 gm. every 4 hours thereafter for the next 24 hours, without any effect on her condition. When seen in consultation, the temperature was 104.8°F., the pulse 160, and the blood pressure 60/40. The patient was acutely ill, breathing with difficulty. There was a diffuse scarlatina-form eruption, and petechiae appeared at any points of trauma. The pulse was thready and rapid, and the abdomen, which was distended, showed marked tenderness in the lower quadrants. A presumptive diagnosis of puerperal sepsis due to scarlatinal hemolytic streptococci was made,

sodium sulfathiazole, the temperature was 99°F. Because of the circulatory collapse, 500 cc. of reconstituted dried plasma was given after the temperature began to fall and the blood pressure rose first to 95/55, when the patient began to void again, and then to 125/80.

A subsequent blood culture, taken before sodium sulfathiazole was given, showed gram-positive diplococci that looked like staphylococci, but were not finally identified. The blood level after the 8 gm. of sodium sulfathiazole was 32 mg. per 100 cc. For the next 17 days sulfathiazole was continued by mouth and the patient made slow progress, despite the development of an acute nephritis, probably due to a combination of sulfathiazole and her infection, and of a spontaneous pneumothorax, which required aspiration of air on repeated occasions. Because she developed some delirium on the 17th day, and there seemed to be no more abdominal tenderness, sulfathiazole was discontinued.

For the next 12 days the patient did very well. However, she then developed pain over the bladder, coming on after voiding. The physician, fearing that she was getting a bladder infection, gave her 1 gm. of sulfathiazole, which was repeated every 4 hours. Despite this, the temperature rose steadily to 104°F., with rapid pulse and respiration. At this time physical examination was negative except for a diffuse bright-red erythema. The white-cell count was 19,000, with 91 per cent polymorphonuclear cells. Questioning revealed that 1 hour after the first dose of sulfathiazole the patient developed epigastric distress and vomited. A diagnosis of drug fever was made, the sulfathiazole was discontinued, and fluids were forced. In 18 hours the temperature had fallen to 102°F. and the

white-cell count to 10,000. Shortly thereafter the temperature rose to 104°F, but the patient felt better. In 36 hours after stopping the drug the temperature became normal and the patient felt entirely well again. From then on, recovery was uneventful.

Comment This case illustrates many points about chemotherapy. First, the patient was given entirely inadequate doses of sulfadiazine when she was obviously suffering from a fulminating case of puerperal sepsis. Therefore, heroic measures were necessary and she was given massive doses of intravenous sodium sulfathiazole. That these were massive was shown by the blood level of 32 mg per 100 cc after 8 gm, due no doubt to the anuria, which resulted from the circulatory collapse with low blood pressure. As a result of this heroic therapy, the temperature fell to normal in 12 hours. The response of the shock state to plasma, which restored both blood pressure and urinary output, was due to the fact that the infection had already been brought under control. The nephritis that followed, characterized by fixed specific gravity, heavy albuminuria and hematuria with many granular casts consisting of masses of sulfathiazole crystals, was typical of the direct renal injury produced by the drug. The final episode of fever on a second administration of sulfathiazole was a typical accelerated reaction due to previous sensitization. The rash, leukocytosis and high fever were sufficiently like the onset of the infection, however, to make the decision difficult.

CASE 7 (PBBH M61859) (Fig 4) This 44-year-old Italian bartender, who had been a heavy drinker for years, caught cold and lost 'pep' and 20 pounds in weight in

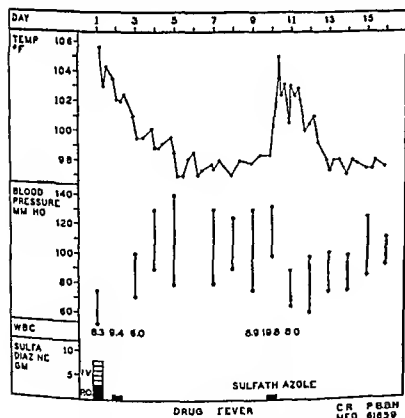


FIGURE 4 Clinical Course of Case 7

the month before admission. Six days before entry he became much worse, with the development of headache, chills, pain in the left side and increased cough with dark blood streaked sputum. Three days before entry he had to take to his bed, because he felt dizzy and exhausted. On admission the temperature was 105.6°F, the pulse 120, the respirations 30, the blood pressure 75/50, and the white-cell count 8300, with a shift to the left. There

were a generalized reddish flush to the skin, muscular aches in both lungs, a little dullness at the right base, abdominal distention and a rapid, weak pulse. On admission a diagnosis of lobar pneumonia was made, and because the patient was so ill, intravenous sodium sulfadiazine followed by oral sulfadiazine was given, and the blood level rose to 14.5 mg per 100 cc. However, since the sputum failed to show pneumococci, a blood culture was negative, and the chest was clear on x-ray examination, the drug was discontinued, and the temperature fell to normal in 3 days with a concomitant rise in blood pressure. An electrocardiogram the day after admission showed intraventricular block, but 5 days later, after intramuscular thiamine therapy, the curves were normal. Therefore, in view of the patient's occupation and his story of loss of strength, a diagnosis of acute beriberi with cardiac manifestations was made in retrospect.

At this point careful questioning of the patient and his physician revealed that he had acquired gonorrhea 2 weeks before entry for which he had been treated with sulfathiazole in full dosage. Shortly before entry he developed fever, and therefore his physician told him to discontinue the drug, but since he became worse he entered the hospital. This made it seem most likely that the patient had severe drug fever on admission. Fortunately, he had been given sulfadiazine, and not sulfathiazole, on entry, or he might have died.

Since it seemed important to know whether the patient was extremely sensitive to the sulfonamides, it was decided to test him with a small dose of each of the drugs. On the 10th hospital day he was given 1 gm (2 tablets) of sulfathiazole. Within an hour the temperature and pulse began to rise, and in 3 hours he had a severe shaking chill lasting 45 minutes. Eight hours later the temperature was 105°F, the pulse 120, and the blood pressure 104/80, and he was acutely uncomfortable, complaining bitterly of headache. The skin was a fiery red and the conjunctivas markedly reddened. High fever continued for 36 hours, with persistence of the rash and a state of circulatory collapse, with the blood pressure about 90/65 most of the time, despite abundant intravenous fluids, 500 cc of plasma, adrenalin and aspirin. An electrocardiogram taken on the 2nd day of the reaction showed paroxysmal right bundle-branch block. On the 4th day after the test dose of sulfathiazole the temperature returned to normal, and on the 6th day the blood pressure returned to its usual level (125/85). The white-cell count rose to 19,800 at the height of the reaction and the next day was 8000, with 92 per cent polymorphonuclear leukocytes. Albumin, red cells and casts were noted in the urine during the reaction. Needless to say, tests were not made with the other sulfonamide drugs.

Comment This case illustrates both how confusing drug reactions may be to the physician who first sees a patient during the reaction, and also how serious they may be, at least with sulfathiazole. This case seems to show that sulfadiazine may be tolerated by patients exquisitely sensitive to sulfathiazole, since this patient improved rapidly when given sulfadiazine intravenously and orally.

Certainly the best diagnostic criteria for drug fever are the absence of other adequate causes for fever and its appearance five to fourteen days after the start of therapy.

VII. What precautions should be observed in the care of patients receiving sulfonamide therapy?

With the substituted sulfonamides now in common use, only three serious toxic reactions occur with much frequency—fever, leukopenia and oliguria. The temperature should be taken at least twice daily to guard against fever. Leukopenia rarely occurs before the tenth day of treatment, therefore, every effort should be made to end treatment by this time, particularly if the patient is ambulatory. After ten days a close check must be kept on the white-cell count, with determinations every two days. Oliguria is most apt to occur in the period of intensive therapy. The appearance of red cells or granular casts in the urine should serve as a warning that this toxic reaction is imminent, but the best precaution is to observe the urine output in twelve-hour periods. When this falls below 800 cc., fluids should be forced intensively. Sulfathiazole, particularly, may cause complete anuria without the appearance of hematuria. Crystals of the drug mean nothing in a routine urine examination, since these drugs crystallize at room temperatures, but the presence of large numbers of crystals in a freshly voided specimen means that the patient needs either more fluids or a smaller dose.

One point that cannot be emphasized too strongly is that leukopenia or drug fever may occur after the administration of a sulfonamide has been stopped. This is particularly true of sulfadiazine, which is the most slowly excreted, and is to be feared in patients with poor renal function, who rid themselves of any of these drugs very slowly. Sulfathiazole, although it produces toxic reactions more often than does sulfadiazine, is excreted very rapidly, so that if a reaction occurs (except oliguria) it is possible to get rid of the offending drug very quickly. This usually produces prompt recovery from the toxic effect (Case 5). On the other hand, with sulfadiazine several days are needed for its elimination. Case 8 illustrates this serious drawback to its use. Because of the possibility of delayed reactions after the cessation of therapy, the white-cell count and the patient's condition should be checked three and five days after treatment is discontinued. Failure to observe this rule will sooner or later lead to trouble.

CASE 8 (P.B.B.H. M62187) (Fig. 5). This 56-year-old woman with a history of chronic sinusitis developed fever and rapid respirations within a few hours of an operation on the 3rd hospital day. By the next morning the temperature was 103°F., the pulse 110, the respirations 40, and the white-cell count 19,000. A practically pure culture of *Staph. aureus* was obtained from the throat (she could raise no sputum). The patient was cyanotic and

there were signs of consolidation in the right lower lobe. A diagnosis of postoperative pneumonia due to *Staph. aureus* was made, and sulfadiazine was given in large doses, starting on the 5th hospital day. Her temperature fell slowly but steadily, in an entirely satisfactory manner for a patient with a staphylococcal infection. On the 17th day the white-cell count was 9000, the chest signs had cleared, and the patient seemed fairly well. Because the temperature still showed some elevation, the dose of sulfadiazine was reduced, as it was difficult to tell whether this fever was due to the drug or to infection. Since the temperature decreased after this, the drug was discontinued on the 21st day. At this time the white-cell count was 5000 and the temperature normal. Two days later the count was still 5000, the temperature still normal, and the patient was sitting up.

On the 26th day the patient complained of slight sore throat and malaise, developed chills, and by the next day her temperature was over 105°F. and she looked very ill. The white-cell count showed 1250 cells, and on smear no polymorphonuclear leukocytes were seen. This was 6 days after chemotherapy had been discontinued. Despite Pentnucleotide, liver extract, transfusion and vitamins B and C, the patient became steadily worse, the white-cell count failed to rise significantly, fever continued, and she died on the 29th day. Autopsy confirmed the clinical impression that the pneumonia had been cured, and revealed hyperplasia of the bone marrow and an acute enteritis. Post-mortem and two ante-mortem blood cultures were sterile. On the day of death the blood sulfadiazine was 0.79 mg. per 100 cc.

Comment. This case proves in a tragic way that serious toxic reactions may occur a considerable time after the period of chemotherapy. The drug was stopped at a time when there was no reason to suspect that anything was wrong. The white-cell count of 5000, although low, was no lower than is frequently seen when a patient is recovering on sulfonamide therapy and was no lower 2 days later. Perhaps the only sign of impending trouble was the slight unexplained fever after the 15th day; but from the 22nd to the 26th day the patient seemed entirely well. The slow excretion of sulfadiazine and its possible dangers are dramatically illustrated by this case.

The following outline presents a recommended routine in using the sulfonamides:

A. Before administration:

1. Inquire about previous sulfonamide therapy and toxic effects.
2. Assess renal function (possible nocturia, frequency, history of nephritis; urinalysis).
3. Determine hemoglobin level and white-cell count.

B. Administration to ambulatory patients (small doses):

1. Instruct the patient about
 - a. Name of drug.
 - b. Importance of regular doses.
 - c. Importance of adequate fluids and check on volume of urine output.
 - d. Possibility of toxic reaction (report untoward episodes).
 - e. Dangers from slow reaction time in crossing streets, driving car and so forth.

2. Arrange check-up visits at 3, 7 and 10 days; after 10 days the patient should be seen three times a week up to 6 weeks, then weekly so long as the drug is continued.

Check-up should include examination of the mucous membranes for pallor, scleras for icterus

particularly anuria, the renal function is apt to be somewhat impaired, so that the blood level should be watched more closely if the drug is readministered. In all toxic reactions the first move after discontinuing the drug should be the administra-

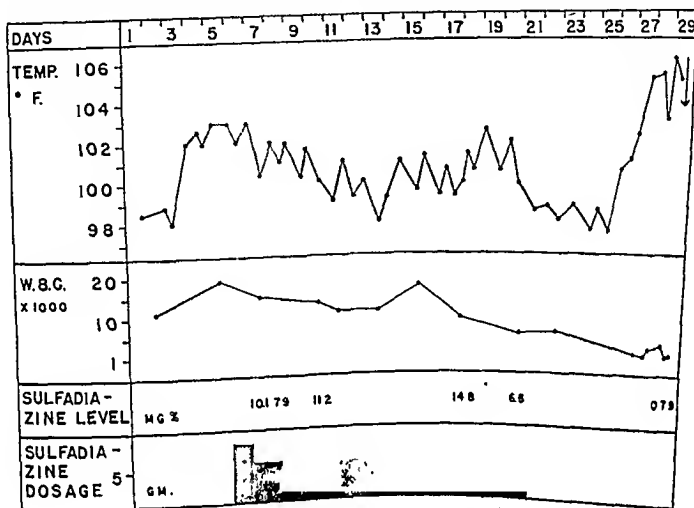


FIGURE 5. Clinical Course of Case 8.

and skin for rash, a temperature reading and inquiry about malaise, nausea and urinary output. If the last is low, urinalysis should be done. A white-cell count should be made, and if below 6000 a blood smear should be examined.

C. Administration to hospital and bed patients (large doses):

1. Instruct patient or nurse about importance of regular doses.
2. Measure urine output in 12-hour lots; perform a urinalysis daily during the acute phase.
3. Watch the temperature chart.
4. Determine the hemoglobin level weekly and the white-cell count three times a week; examine a smear weekly.
5. Examine patient daily, noting conjunctivas (pallor), skin (rash, purpura), scleras (jaundice), general appearance and behavior.

VIII. What should be done if a toxic reaction occurs?

Acute hemolytic anemia, purpura, hepatitis, high fever, severe rash and leukopenia are indications for immediate cessation of chemotherapy. Oliguria is an indication for omitting one or two doses until an adequate output returns. Following o-

tion of a large amount of fluid (6 liters a day), to hasten the excretion of the sulfonamide. If evidences of infection return with the cessation of chemotherapy, several courses are open to the physician. First, do nothing if the infection is mild. Second, when the infection is severe, use serum or some other type of therapy if it is available. Third, try a different member of sulfonamide group, using a 0.5-gm. trial dose allowing twelve hours to elapse if possible. Adequate figures are available on the frequency with which reactions occur with the other sulfonamides if a toxic reaction occurs with one of them. In some cases it is possible to change from thiazole to sulfadiazine (Case 7) without any trouble. In other cases sensitivity to a member of the group seems to be sensitivity to some or all of the others.

The treatment of agranulocytosis is unsatisfactory. All that can be done is to promote excretion, and to give small injections of Pentnucleoside extract, both of which may count for a stimulation of the bone marrow.

life, and some observers think that repeated transfusions may depress the bone marrow.

If anuria occurs as a result of sulfonamide therapy, fluids should be forced, and sufficient sodium bicarbonate given to bring the blood-bicarbonate level to normal if it is depressed. If no urine appears as a result of these measures, the ureters should be catheterized and lavage with mildly alkaline solution given as high as possible to dissolve and break up any calculi or precipitates in the ureters and pelves. This has been more successful with sulfapyridine than with sulfathiazole, which is apt to produce more damage in the kidney itself.

SUMMARY

The following directions are suggested in sulfonamide therapy:

Do not give sulfonamides without good indications.

Do not withhold sulfonamides from desperately ill patients with undiagnosed infections.

If sulfonamide therapy is elected, use adequate doses.

If a patient is very seriously ill, begin with an initial intravenous dose of the sodium salt of the sulfonamide to be used.

Try to cure the patient in the first few days before toxic reactions confuse the issue.

Continue therapy for two or three days after all evidences of active infection subside, or until adequate localization occurs. In meningitis and deep infections involving bone, chemotherapy should be continued longer after apparent cure.

If no response to therapy occurs in two days, check the diagnosis, check the sulfonamide blood level, look for pus, and suspect drug fever.

If no response occurs to *adequate* therapy in three days, discontinue the drug.

Before administering sulfonamides, try to find out whether the patient has had them and had reactions previously.

Try to assess renal function before deciding on the dosage.

Watch for serious reactions, checking the white-cell count, particularly after ten days, and watching the urine output.

Continue to watch the white-cell count for a week after treatment is stopped.

Force fluids with all drugs but sulfonamide.

After the patient is cured, tell him which sulfonamide drug he has received; if he has had a reaction, instruct him to inform any physician about it before taking sulfonamides again.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28531

PRESENTATION OF CASE

A twenty-four-year-old nulliparous waitress entered the hospital complaining of abdominal pain of two weeks' duration.

One year before entry the patient had a two weeks' episode of pain in the right and left lower quadrants without chills, fever, nausea or vomiting. She was treated at a community hospital for five days with hot douches, and was apparently cured. She was perfectly well until two weeks before entry when she suddenly experienced throbbing pain in the left lower quadrant of the abdomen. The pain was not severe enough to double her up, but it persisted steadily for six days and then abated somewhat. On the third day of this attack her physician found that she had a temperature of 101°F., and gave her "large white pills," of which she took two every four hours for five days. The drug was stopped because of nausea and vomiting. Four days before entry she had an exacerbation of the pain, which continued until admission. She had had no gastrointestinal or genitourinary symptoms. She had lost about 15 pounds in the previous two months. Her last menstrual period had begun just after the onset of the pain.

She had had the usual childhood diseases. When eight years old she spent a year at a tuberculosis sanatorium because of a "swollen belly." She had several abdominal paracenteses there, and was told that her trouble was due to drinking unpasteurized milk. She had had an appendectomy four years before entry, and an operation for elephantiasis three years before.

She was married when eighteen years old and was separated eighteen months later, but admitted sexual intercourse since then.

Physical examination showed an obese woman with five operative scars, two in each thigh and one in the right lower quadrant. Examination of the heart and lungs was negative. The lower abdomen was prominent, especially on the left, where there was marked tenderness with questionable spasm. There was no tympany, and peri-

stalsis was normal. There was a large rounded lower abdominal mass, which seemed to reach to the umbilicus. The liver was felt one finger-breadth below the right costal margin. The spleen was not palpable. Pelvic examination showed a marital introitus, slight leukorrhea and a normal nulliparous nontender cervix. There was marked tenderness in both vaults, and the fundus could not be felt because of the extreme tenderness. The abdominal mass was tender and did not seem to be connected with the cervix. Rectal examination confirmed the vaginal findings.

The temperature was 100°F., the pulse 64, and the respirations 20. The blood pressure was 96 systolic, 52 diastolic.

Examination of the urine was negative except that the sediment showed 15 to 20 white cells per high-power field; a culture was negative. The blood showed a red-cell count of 4,700,000 with a hemoglobin of 90 per cent, and a white-cell count of 8800 with 76 per cent polymorphonuclears. A cervical smear was negative for gonococci. A blood Hinton test was negative. A tuberculin test (1:100,000) showed a 3-cm. area of erythema at the end of forty-eight hours. An Aschheim-Zondek test was negative.

An abdominal roentgenogram showed a huge soft-tissue mass in the abdomen rising to the level of the first lumbar vertebra and swinging to the left. There was an indefinite area of calcification overlying the left side of the fourth lumbar vertebra, and a similar indistinct area of calcification overlying the left twelfth rib. The areas of calcification appeared to lie peripherally about the mass. An intravenous pyelogram was negative. The mottled calcification seemed to lie over the upper pole of the left kidney but was shown to shift its position relative to the kidney calyces. The bladder film showed a pressure defect that almost obliterated the left half of the bladder. Following a barium enema, the sigmoid was seen to be displaced and plastered against the abdominal mass.

An operation was performed on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. GRANTLEY W. TAYLOR: We are concerned with a young woman who presented a large abdominal tumor that had given rise to symptoms of only two weeks' duration.

The past history almost certainly establishes that she had tuberculous peritonitis in childhood, from which she apparently recovered completely. A

laparotomy for appendicitis four years previously would presumably have disclosed persistent disease if it had been present, and might also have revealed the tumor if it had been of long standing. Nothing is offered regarding a possible explanation for the development of elephantiasis in a woman who required operation at the age of twenty-one. In this connection it would be of interest to know her race and nativity. It must be assumed that at some time she suffered from a thrombophlebitis resulting in obliteration of the lymphatic pathways. This may have occurred during her hospitalization in childhood, or possibly following her appendectomy. A year before admission she had an episode of lower abdominal pain, which was probably due to an acute pelvic inflammation.

It is difficult to picture that any of these previous illnesses had any bearing on the tumor. Tuberculosis may give rise to large lymph nodes or inflammatory masses in the abdomen, and these may be associated with calcification, as shown in the x-ray films. But if these had occurred, symptoms would undoubtedly have been present over a longer period, and it would be most unusual for such a large mass to have been present. It is conceivable that a pelvic tumor by pressure could have given rise to the elephantiasis of the thighs, but under these circumstances there would have been numerous other related symptoms. Very large pus tubes may sometimes follow acute pelvic inflammation, but they never achieve the size of this tumor and would undoubtedly present more symptoms in the course of their development.

Other types of inflammatory masses in the abdomen might be mentioned, such as a large hydro-nephrosis or pyonephrosis and the inflammation surrounding diverticulitis of the sigmoid, but there were no other signs and symptoms suggesting the presence of such conditions.

May we have the x-ray films?

DR. JAMES R. LINGLEY: This mass is very large, filling the lower abdomen and extending out to the left flank. It is uniform in density throughout and has sharply defined, smoothly rounded borders without lobulation. It displaces the sigmoid medially but does not involve the bowel.

There are at least six areas of calcification in the abdomen, all of which lie outside the large mass. The four in the upper abdomen have the typical appearance of calcified mesenteric tuberculous lymph nodes. The lower two, however, are unusual in two respects, if they are nodes. First, their positions are wrong, as one lies well out in the right flank and the other lies anteriorly immediately against the anterior abdominal wall.

Secondly, their density is uniform throughout and is much less than one expects in a tuberculous node. Their density and structure suggest the calcification sometimes seen in a certain tumor that occasionally involves the peritoneum extensively.

The film of the chest shows normal lungs, but the diaphragm is elevated, particularly on the right.

DR. TAYLOR: Are the psoas muscles normal?

DR. LINGLEY: Yes; and the kidneys and ureters are not remarkable.

DR. TAYLOR: By x-ray the area of mottled calcification was said to move independently of the kidney, and there were no symptoms referable to the genitourinary or gastrointestinal tract.

An echinococcus cyst must be mentioned as a possibility. Again knowledge of the race and nativity of the patient would be helpful. No specific tests were carried out. Presumably an eosinophilia would have been noted in the blood smear if it had been present.

When we come to consider the various cysts and tumors that may occur in the abdomen, we are at once impressed with the silent character of the tumor prior to the acute episode. The position of the tumor in relation to the side of the bladder, as shown by the x-ray films, argues for a pelvic origin, rather than a tumor involving the liver, spleen or kidney. A cyst of the mesentery or omentum may be present in the pelvis, but does not result in the lower abdominal and vault tenderness. Fibroids and ovarian and paraovarian tumors and cysts are the most likely masses to consider.

Regarding a fibroid tumor, the patient was young, the mass seemed independent of the cervix, and there was no abnormal menstrual history. These do not necessarily rule out fibroid, but tend to. Between solid and cystic ovarian masses, the large size of the tumor argues for a cyst, as does the absence of early symptoms of pressure.

An explanation of the acute episode, with pain, fever and tenderness, must be offered. It seems probable that there had been some torsion or interference with the blood supply to explain these symptoms. In my opinion, the preoperative diagnosis is ovarian cyst, with a torsion of the pedicle. The areas of calcification shown in the x-ray films may have been residuums from the old abdominal tuberculosis, or they may have been areas of calcification in the cyst itself.

DR. LINGLEY: I do not believe that all the calcification is typical of either calcified tuberculous mesenteric nodes or of the tumor I mentioned, namely, papillary cystadenocarcinoma of the ovary. It is quite possible that all the calcification is tuberculous in nature, but in view of the large mass, which is probably a cyst of the ovary, I suggest that the entire picture may have been due to papil-

lary cystadenocarcinoma of the ovary, with extensive osammoma calcification throughout the abdomen. I should be much happier about the latter diagnosis if there were psammoma calcification within the large mass itself.

DR. LOWREY F. DAVENPORT: What about the palpable liver?

DR. TAYLOR: I do not believe that is significant in the presence of obesity.

DR. CLAUDE E. WELCH: I should cast doubt on the past history of elephantiasis, inasmuch as only the thighs were involved.

DR. JOHN H. TALBOTT: I should like to offer one diagnosis that probably does not contribute to the principal difficulty in this patient. The past history of tuberculosis, the presence of hypotension and the roentgenograms of the abdomen showing calcification over the upper pole of the right kidney make one consider Addison's disease. If I had seen only the plain films of the kidney, both anteroposterior and lateral, I should have called it atypical of calcified adrenal tissue and highly suggestive of Addison's disease. Of course in consideration of the entire picture one is foolish to make a diagnosis of Addison's disease, but I do believe that the patient is a likely candidate for that disease in the future. She may well develop a lesion of the left adrenal gland in addition to that of the right, which is demonstrable now.

DR. LINGLEY: I agree that there is one small area of calcification in the region of the right adrenal gland, but I doubt that it is in the gland since it moves independently of the kidney, and in the lateral view lies anterior to it.

DR. ALFRED KRANES: Should a mesonephroma be considered?

DR. LINGLEY: I am not familiar with that condition.

DR. DONALD S. KING: Could this be a tuberculous mass?

DR. TAYLOR: I have never seen a tuberculous mass reach this size.

DR. JAMES H. TOWNSEND: I believe that tuberculous salpingitis can sometimes result in the formation of a mass of this magnitude.

CLINICAL DIAGNOSIS

Ovarian cyst.

DR. TAYLOR'S DIAGNOSES

Ovarian tumor, probably a cyst, with torsion.
Old tuberculous peritonitis.

ANATOMICAL DIAGNOSES

(Pseudomucinous cyst of ovary.)
Encapsulated tuberculous peritonitis with calcification.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was operated on by Dr. Burbank, and I shall ask him to describe his findings.

DR. CHARLES B. BURBANK: Our preoperative diagnosis was ovarian cyst. At the time of operation about 2500 cc. of clear yellow fluid under some pressure was found free in the peritoneal cavity. The entire lower abdomen was filled with a large cystic mass, which was adherent to the anterior abdominal wall at the level of the symphysis pubis and also to the right iliac fossa. On the other side it extended almost to the left iliac fossa. Its upper border was at the level of the umbilicus. It had pushed the small intestine forward, and many coils of the ileum were adherent to its anterior and lateral walls and also to each other. It was impossible to enter the pelvis or to identify any of the pelvic organs. Lying just below the peritoneum at the upper end of the incision was a separate mass, measuring 5 by 4 by 2 cm., with a yellow surface. It was soft in consistence and when opened contained white material suggestive of tooth paste. This was totally excised.

Since it was obviously impossible to free up the large cyst, the wisest procedure appeared to be to drain it through the abdominal wall. When an incision was made into it, a large amount of clear fluid was evacuated. A segment of the wall was removed. The inner surface of the cyst was smooth. It was my impression that it was a pseudomucinous cyst, presumably of the right ovary.

DR. MALLORY: In none of the material submitted to the laboratory could we positively identify the cyst as ovarian in origin. However, I think Dr. Burbank's impression can be accepted with reasonable confidence. The smaller mass proved to be an encapsulated mass of semicaseous exudate with active tubercle formation in some portions of its wall and many foci of calcification, 50 to 200 mm. in diameter, in other areas. Many of these were not larger than psammoma bodies, so it is natural that the x-ray picture should have suggested an ovarian papillary cystadenoma to Dr. Lingley.

CASE 28532

PRESENTATION OF CASE

A twenty-one-year-old girl entered the hospital complaining of chills and fever of two and a half weeks' duration.

At nine months of age the patient had been seen at another hospital because of fever and vomiting. The outstanding and relevant findings at this time

were a temperature of 103°F., a pulse of 190 and a respiratory rate of 60. The heart was markedly enlarged to the left with a blowing systolic murmur all over the precordium, but heard best at the apex and transmitted to the back; the enlargement was verified by x-ray examination. At the end of a month the heart had decreased in size, the left border being only 6.5 cm. from the mid-sternal line, with the apex in the fifth interspace. She was discharged two days later with a normal temperature and respirations, but the cardiac murmur had persisted. The patient was readmitted to the above institution two months later with a temperature of 102°F., and a pulse of 150. The same cardiac findings were recorded, the left heart border varying from 8.5 to 9.5 cm. from the mid-sternal line. No significant signs were noted in the lungs, nor was there clubbing of the fingers. During the next two years the patient was examined in the outpatient department of the same hospital at infrequent intervals. The same cardiac abnormalities were noted, and during this period she suffered from urticaria, nasopharyngitis and tonsillitis, the last of these being eliminated by an adenotonsillectomy.

At the age of sixteen, the patient was first seen in the Cardiac Clinic of the Out Patient Department of this hospital, and she continued her visits until the time of admission. No history of rheumatic fever could ever be obtained, and the patient denied having had sore throats, joint pain, chorea, fever, nosebleeds, dyspnea and cardiac arrhythmia, although she suffered from about three head colds each year. The following is a summary of the findings during this period. The patient's appearance was always rather delicate and sickly. The heart was markedly enlarged, the impulse heaving, without a palpable thrill, and the rhythm regular at a rate averaging 100. The sounds were tumultuous, with a loud systolic murmur at the apex replacing the first sound and transmitted to the left lung base. During these years an apical mid-diastolic murmur was thought to be present by some examiners, usually brought out by exercise. The blood pressure averaged 95 systolic, 75 diastolic. Occasionally rhonchi were heard at the lung bases, but at no time were there subcutaneous nodules, clubbing of the fingers or a palpable spleen; a tendency to cyanosis after exercise was very questionable. Three years before admission an x-ray film of the chest showed a heart that was grossly abnormal in shape, with an unusually prominent left upper border. The aorta was small, and the pulmonary vessels dilated. The peripheral lung fields were clear, and the diaphragm was low. Another x-ray examination two years later showed that the heart was enlarged to

the left as well as in the anteroposterior diameter, with a questionable enlargement of the left auricle. The pulmonary conus was prominent, and the hilar vessels and vessels within the lung parenchyma were wider than usual. Fluoroscopy was performed six months before admission and showed enlargement of both the right and left ventricles, with a cardiothoracic ratio of 12:19. The pulmonary conus was enlarged, and a considerable degree of pulsation was seen in the pulmonary arteries. There was no significant enlargement of the auricles. An electrocardiogram at this time showed normal rhythm, a rate of 90 and a PR interval of 0.19 second. T₃ was flat; the QRS voltage was unusually high in Leads 2 and 3, and its amplitude widened to 0.12 second. There was no abnormal axis deviation.

During all this time the patient led a quiet life and remained fairly well, although she entered the hospital for six days on one occasion suffering from severe gingivitis, which cleared readily on treatment.

Two and a half weeks before entry the patient "caught cold"; the onset was accompanied by malaise, anorexia, a persistent cough and chills, and was followed by a low-grade fever. She went to bed and during the next three days had several more chills; at the end of this period, however, the temperature fell to normal and she felt better. The patient resumed her usual activities, but one week before admission a severe chill occurred, which was followed by a temperature varying from 99 to 104°F. In bed again, she suffered from a series of shaking chills with occasional night sweats, and thirty-six hours before entry, at four o'clock in the morning, a severe chest pain awakened her from sleep. This pain was sharp, located in the right chest posteriorly, was aggravated by deep breathing and coughing, gradually increased, but was relieved somewhat by hot packs.

The patient's mother had had rheumatic fever and tuberculosis, and one sister had tuberculosis of the spine.

On examination, the patient was thin, poorly developed and appeared chronically ill, with pale, shiny skin, slight mucous-membrane cyanosis, slight clubbing of the fingers with floating nails and a definite increase in the volume of the jugular pulse. Examination of the head and neck was negative. The lungs were clear. The heart was enlarged, the border being 1.5 cm. to the right of the midsternal line with the apex palpable at the anterior axillary line in the sixth intercostal space. The apex impulse was rapid, regular and forceful; no thrills could be felt. There were two low-pitched murmurs at the apex,—a loud systolic and a rumbling diastolic,—the former being

transmitted to the left lung base. In addition, a high-pitched and loud systolic and a short mid-diastolic murmur were heard just to the left of the lower sternum. These last two murmurs were rather distinctive, but could not be separated definitely from those at the apex. The liver was just palpable, and the spleen easily palpable. Vaginal and rectal examinations were negative.

The blood pressure was 95 systolic, 65 diastolic. The temperature varied between 99 and 105°F. The pulse averaged 100, and the respirations 27.

Examination of the urine was negative. The blood showed a red-cell count of 4,300,000 with a hemoglobin of 13 gm. and a white-cell count varying between 9000 and 18,000, of which 75 per cent were polymorphonuclear leukocytes. Repeated blood cultures yielded Type 6 pneumococci. The nonprotein nitrogen of the blood serum was 26 mg. per 100 cc. The blood Hinton reaction was negative. The stools were normal.

An electrocardiogram showed a normal rhythm with a rate of 115 and a PR interval of 0.20 second. The QRS complex in Leads 2 and 3 was M shaped and low.

An x-ray film of the chest showed gross cardiac enlargement, apparently in the region of the right ventricle and pulmonary artery. Also, there was slight dilatation of both auricles. The aorta was unusually small, whereas the pulmonary vascular shadows were increased in number and size. There were no areas of consolidation in the lungs, and no fluid at the bases. Fluoroscopically, a hilar "dance" was noticed.

Throughout the patient's illness chemotherapy was used, starting with sulfadiazine, which reached a blood level averaging 12 mg. per 100 cc. However, by the thirteenth hospital day, this level had climbed to 21.2 mg. so the drug was discontinued, and the next day the concentration dropped to 15.9 mg. During the last few days of life a shift from sulfadiazine to sulfathiazole was made because the patient had failed to respond to the former drug.

The first few days of hospitalization were without incident, but six days after admission the patient developed a headache, but remained clear and co-operative. Examination showed a widely dilated left pupil, which failed to react, and a third-nerve paralysis on the left, the patient being unable to open the eyelid. A lumbar puncture revealed no abnormalities. She was given 100,000 units of Type 6 antipneumococcus rabbit serum intravenously in four hours, after a negative Francis test. The next day an additional 60,000 units was administered. Four days later the patient developed slight weakness of the seventh left cranial nerve, with a slightly stiff neck and a pos-

itive Kernig sign. Two weeks after admission, pain on respiration developed in the right lower chest anteriorly, with slight cough and dyspnea but no sputum. Examination revealed a few rales and a slight rub low in the right axilla at the end of inspiration. Death occurred on the eighteenth hospital day after an increase in cyanosis and the development of puffiness of the face and moist rales bilaterally. Bronchovesicular breathing with increased whispered voice sounds was heard over an area 4 cm. in diameter at the left lung base.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD F. BLAND: First I should like to ask Dr. Sullivan to comment on the Francis test and its significance.

DR. EUGENE R. SULLIVAN: The Francis test depends on the reaction between the type-specific soluble carbohydrate extracted from the capsule of the pneumococcus and its corresponding antiserum. By injecting intradermally a small amount of the specific carbohydrate (in this case, Type 6), one can test for the presence in the blood of Type 6 pneumococcus antibodies, either of natural development or artificially administered. A positive skin reaction is frequently used as a guide to indicate that enough antiserum has been given.

DR. BLAND: There are two diagnostic problems presented by this case: the answer to the first is evident, but that to the second is difficult.

In connection with the first, the clinical course indicates clearly that this patient succumbed to a pneumococcal septicemia associated with acute bacterial endocarditis superimposed upon previously existing heart disease and complicated by pulmonary infarcts (presumably septic) and by either a metastatic brain abscess or meningitis—probably a combination of the two. A special feature of the embolic phenomena will be commented on later, since it may prove helpful in trying to unravel the second, and more difficult, feature of the case—namely, the underlying type of cardiac disease and especially the structural defects present within the heart.

Any patient in the vicinity of Boston with chronic heart disease in this age group deserves, first, a most careful scrutiny for evidence of rheumatic heart disease, since in this part of the world rheumatic fever is responsible for more than 95 per cent of the crippled hearts in young people. However, I do not believe in this case we have sufficient evidence to consider seriously this etiologic factor. In the first place, the existence of heart disease was recognized at the age of nine months. This is unusually early for the onset of rheumatic fever, although rare cases have been recorded even

in infancy. The youngest patient I have personally observed with rheumatic fever was fourteen months old. The absence of an illness recognizable as rheumatic fever in this patient is only moderately helpful in a negative direction. Of considerably more importance in excluding a rheumatic factor, I believe, are the physical signs, which are not in accord with the more or less well-defined pattern presented by chronic rheumatic scarring of either the mitral or of the aortic valve, and the appearance of the electrocardiogram, which in this instance is particularly suggestive, not of rheumatic heart disease, but of a congenital cardiovascular defect. On these grounds I am therefore willing to discard rheumatic heart disease from further consideration.

I believe we are concerned with a congenital defect in the heart, possibly a combination of such defects. The problem is to name the condition, for we no longer consider it adequate to dismiss such cases with the broadly inclusive term of "congenital heart disease." Experience has shown that an accurate structural diagnosis is possible in the majority of those who survive the first few months of life. A definitive diagnosis in these cases is of considerably more than academic interest for it determines within limits the prognosis, and in an occasional case leads to corrective surgery.

May we have an interpretation of the x-ray films at this point? I notice from the dates that the films submitted are those taken approximately six months before death, when the patient was in relatively good health. The films taken during the final illness are, unfortunately, not available.

DR. JAMES R. LINGLEY: The films taken six months before death show clear lung fields. The heart shadow is grossly abnormal in size and shape. The enlargement is predominantly ventricular, and it appears to affect the right side more than the left. The aorta is hypoplastic as shown by the absence of the curve of the ascending portion along the right upper mediastinum and by the inconspicuous knob. The pulmonary conus is very prominent, and the pulmonary artery is dilated. There is also dilatation of the vascular shadows throughout both lungs, and fluoroscopically a hilar "dance" was demonstrated. So far as I know, this occurs only in congenital heart disease, and most commonly in association with a patent ductus arteriosus or an interauricular septal defect.

DR. BLAND: To me these films indicate primarily three things: prominence of both the right and left ventricles—this is supported by the absence of either right-axis or left-axis deviation in the electrocardiogram and hence relatively little disproportion between the two ventricles; little or no enlargement of the auricles; and a striking in-

crease in the amount of blood in the pulmonary circulation.

These findings suggest a shunt within (or near) the heart. If my major premise is correct, namely, that we are dealing with a congenital heart, then the absence of cyanosis (except of slight extent terminally) indicates that the shunt involves a flow of blood from the left (arterial) to the right (venous) side of the heart. This in turn would explain the dense vascular shadows in the lung roots, and the later pulmonary signs (infarcts).

In regard to the location of the shunt, there are three possibilities. The first is a patent ductus arteriosus, which I am inclined quickly to exclude because of the absence of the characteristic physical signs and no widening of the systemic pulse pressure. The second is a large interauricular septal defect, which with some hesitation I am also willing to discard, at least as the major anomaly, largely because of the absence of x-ray evidence of right auricular enlargement, and also because of the absence of right-axis deviation in the electrocardiogram. The third possibility, a defective interventricular septum, seems to me by far the most likely diagnosis. To be sure the murmurs described do not accord with the classic midsternal systolic murmur accompanying septal defects that are small, that is, less than 1 cm. in diameter. In this case, however, I should expect a large defect to be present because of the cardiac enlargement, the large amount of blood in the pulmonary circulation, and especially the appearance of the electrocardiogram. The last, as you recall, showed a wide amplitude of the QRS complexes in Leads 2 and 3, with unusually prominent and deep S waves together with a slight degree of intraventricular block. In fact, this electrocardiogram is so strikingly similar to that of a boy with a single ventricle whom we studied in this hospital about ten years ago that I am tempted to suggest that rare possibility in this case.

A word remains to be said about the final illness. Patients with congenital defects, especially of the interventricular septum, frequently succumb to superimposed bacterial endocarditis, most often subacute in nature and caused by *Streptococcus viridans*. Less often this infection is due to *Str. haemolyticus*, *Staphylococcus aureus* or a pneumococcus, in that order of frequency, and if so, the course is more acute—two to six weeks. Since the abnormal flow of blood is from left to right in the heart, it should be remembered, emboli are swept backward into the pulmonary circulation, with resulting infarction in the lungs. This is my interpretation of the intermittent acute pulmonary symptoms of which this patient com-

plained and which toward the end were associated with signs of pulmonary consolidation

How are we to explain the cerebral symptoms? Was this a paradoxical embolus toward the end as the pressure gradient between the two ventricles declined, and the pulmonary circulation became more engorged? Or was there in addition a complicating interauricular septal defect that permitted passage of an embolus under similar circumstances? I do not know, but I think a more likely explanation is extension of the bacterial vegetations into the left side of the heart with resultant peripheral emboli. Perhaps there was meningitis secondary to the septicemia per se.

To summarize briefly, I believe this patient had congenital heart disease—a large interventricular septal defect (essentially a single ventricle)—and acute bacterial endocarditis, predominantly in the right side of the heart, involving the defect and almost certainly the adjacent cusps of the tricuspid valve with septic infarcts in the lungs and probably in the brain, associated with meningitis. Dr Heyl, would you comment on the neurologic aspects of the case?

DR HENRY L. HEYL The significance of a unilateral third nerve palsy is often obscure. It could represent a local lesion in the region of the nucleus, such as infarct, abscess or thrombosis. It could be caused by a local meningitis secondary to the bacteremia. It might even be due to a contralateral mass pushing the brain to the left and catching the nerve between the tentorium and the cerebral peduncle. Of all these, the presence of a local meningitis seems most likely in this case, with or without a small, precisely placed infarct in the region of the third nerve nucleus. The appearance of the seventh nerve palsy may have represented a spread of infection or a repetition of infarction, however, it was more likely a nonspecific cerebral manifestation of terminal disease.

DR JAMES H. TOWNSEND Would you comment on what you consider the most important signs in patent ductus arteriosus?

DR BLAND A continuous murmur to the left of the upper sternum usually accompanied by a systolic thrill.

DR S. PETER SARRIS Can pulmonary regurgitation give a hilar dance?

DR BLAND Yes, but organic pulmonary regurgitation is extremely rare.

CLINICAL DIAGNOSES

Congenital heart disease (? cor triloculare)
Acute bacterial endocarditis (Type 6 pneumococcus)
Acute meningitis (Type 6 pneumococcus)
Bronchopneumonia

DR BLAND'S DIAGNOSES

Congenital heart disease interventricular septal defect large (? cor triloculare, with a single ventricle)
Acute bacterial endocarditis (Type 6 pneumococcus, involving septal defect and tricuspid valve)
Infarcts, septic lungs and ? brain
Meningitis

ANATOMICAL DIAGNOSES

Congenital heart disease interventricular septal defect, very large (cor triloculare biatriatum)
Bacterial endocarditis, subacute, tricuspid (Type 6 pneumococcus)
Endocarditis, chronic, tricuspid
Pulmonary embolism, multiple
Dilatation of pulmonary artery
Hypoplasia of aorta
Cardiac hypertrophy
Pulmonary edema
Hydrothorax
Infarcts of lung, spleen and kidneys
Hypertrophic pulmonary osteoarthropathy, minimal

PATHOLOGICAL DISCUSSION

DR TRACY B. MALLORY The first suggestion that this patient was suffering from congenital heart disease came from Dr Schatzki, following x-ray examination. Before that time everyone had accepted the diagnosis of mitral stenosis. When the cardiologists were called in consultation they, too, were inclined to congenital heart disease, Dr Ashton Graybiel favoring an interatrial septal defect and Dr P. D. White an interventricular one. In fact Dr White whose note I shall read, hit the nail directly on the head like Dr Bland by suggesting a triloculate heart with a single ventricle.

This is an acute type of bacterial endocarditis not responding to chemotherapy as yet. The problem concerns the diagnosis of the underlying heart disease. Certainly the findings do not fit any of the ordinary types of congenital heart defects such as patent ductus, ventricular septal defect, auricular septal defect, coarctation of the aorta, tetralogy of Fallot and aortic or subaortic stenosis and yet the early age at which the heart disease was discovered (nine months), the bizarre electrocardiogram (wide QRS waves with very prominent R and S deflections in Leads 2 and 3) and odd x-ray picture support the diagnosis of congenital heart disease. Because of the similarity in certain respects (electrocardiographic murmurs and terminal cyanosis) with our one case of triloculate heart with a single ventricle I should hazard that diagnosis here. The next best bet is a very unusual rheumatic heart with early development of mitral and perhaps also

The first health unit was opened on Blossom Street in 1916. Dr. Wilinsky, who was already an official of the Boston Health Department in charge of the West End Health District, became the director of the unit, and under his able leadership the project soon proved its value.

Although improved in succeeding years, the quarters of the unit, consisting of a hall that had been used for a ward-room and subsequently as a gymnasium, were totally inadequate, according to present-day standards. Furthermore, expansion of the program by the provision of additional units in congested districts was slow on account of the expense and of the opposition of those who were not sympathetic.

Dr. Wilinsky always stressed the point that the units should not duplicate the work of clinics. On the contrary, he believed that they should decentralize the services of the Health Department and make them more readily available to the public. Year after year, confidently and persistently, he explained the health-unit idea and gained additional supporters. He convinced the Mayor's Office, the Advisory Board of the Health Commissioner, the Boston Health League and several medical and other groups that had opposed him at first. But it was not until the trustees of the George Robert White Fund became interested in the program that fine buildings were constructed to house the units. The projected series of units was finally completed in 1933.

The fame of the health units has spread far and wide. They have been visited and admired not only by health officials from other American cities, but also by leading sanitarians from many of the countries of Europe. It can truly be said that from Dr. Wilinsky, more than from any other, came the vision, the energy and the enthusiasm that gave Boston these health units. With the passing years will come perspective by which their value can be accurately appraised. It seems likely, however, that they will ultimately be regarded as one of the greatest contributions of this generation to public-health administration.

MEDICAL EPONYM

EUSTACE SMITH SIGN

This sign, although not unanimously accepted as valid, is still frequently referred to. It was described by Dr. Eustace Smith (1835-1914), physician of the East London Children's Hospital, in a communication, entitled "On the Diagnosis of Enlarged Bronchial Glands in Children" (*Lancet*, 2: 240, 1875). He writes:

The symptoms by which enlargement of the bronchial glands can be distinguished . . . are all pressure signs due to the encroachment of the swollen body upon the parts around. . . . At an earlier period, and before the enlargement has become . . . great, . . . much assistance can be gained from the following experiment. If the child be made to bend back the head so that his face becomes almost horizontal and the eyes look straight upwards at the ceiling above him, a venous hum, varying in intensity according to the size of the diseased glands, is heard with the stethoscope placed upon the upper bone of the sternum. As the chin is now slowly depressed, the hum becomes less loudly audible, and ceases some time before the head is brought back again into the ordinary position.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

SURGICAL COMPLICATIONS

Of the 10 deaths that resulted from surgical complications, 5 were due to appendicitis and peritonitis, 3 followed intestinal obstruction, and 2 were associated with ovarian cysts. There were two autopsies.

Of the 5 cases complicated by appendicitis and peritonitis, the first occurred in a primipara who at three months was operated on for symptoms of acute appendicitis of unstated duration. At operation the appendix was found to be ruptured and there was free pus in the abdominal cavity, because of which drains were left in the abdomen. General peritonitis resulted, and death occurred on the fifth postoperative day. The chief question is how long this patient suffered before operation. Too often the symptoms of appendicitis are not recognized, because of pregnancy, until rupture has occurred. Whether or not pregnancy exists, appendicitis should be treated surgically as soon as a diagnosis has been made, and the sooner an operation is performed, the less chance there is of fatal peritonitis.

The second patient, who had had one previous pregnancy, had what were described as "bearing-down pains" in the abdomen and nausea at five months. These complaints continued for two days, at the end of which time a threatened abortion was diagnosed. The following day the patient had a temperature of 100°F. and a rigid abdomen. A diagnosis of acute appendicitis was made, the patient was hospitalized, an unruptured appendix was removed, and the abdomen was drained. She was transfused two days later, and the following morning a spontaneous abortion occurred. Death followed in two days from peritonitis. It is possible that if a diagnosis of acute appendicitis had been made at the onset of this illness and operation performed immediately, this fatality might have been averted. The abortion following operation was probably due to the infection rather than to the operation itself. It must always be borne in mind that a pregnant woman may have acute appendicitis and that this condition demands immediate operation—the sooner this treatment is carried out, the surer one may be of recovery.

The third case occurred in a primipara who had been seen prenatally and who, at about five and a half months, complained of pain in her back, which followed a fall. The temperature and pulse were said to be normal. The following morning she was seen because of pain in the abdomen and a white-cell count of 25,000. An acute gangrenous appendix was removed; three days after the operation the patient miscarried, and she died of peritonitis on the eleventh postoperative day. It is, of course, quite likely that the pain in the back of which the patient complained, regardless of a normal temperature and pulse, was really due to a retrocecal appendix. It is unlikely in an adult that, with a white-cell count elevated to 25,000 and a gangrenous appendix, there were only a few hours of symptomatology. This again emphasizes the importance of early diagnosis of appendicitis.

The fourth patient was a primipara who was delivered at term of a normal living infant but died on the fifth post-partum day of peritonitis. No operation was performed, but an autopsy revealed a perforated gangrenous retrocecal appendix and peritonitis. This was a most regrettable death.

The fifth case was that of a patient who had had six previous pregnancies and was operated on at approximately the fifth month for what was thought to be an ovarian cyst. Operation revealed an acutely inflamed retrocecal appendix, which was removed. The patient's convalescence was febrile and associated with vomiting and distention. Ten days after the first operation the abdomen was again opened and a gangrenous cecum and pelvic abscess were found. The patient went

steadily downhill and died two days after the second operation. The surgery in this case cannot be commended. Undoubtedly this was an entirely unnecessary death.

Three deaths were associated with intestinal obstruction. The first case was that of a patient, six months along in her second pregnancy, who became acutely ill with nausea, vomiting and abdominal pain. A diagnosis of intestinal grippé was made; the vomiting persisted, and the patient was hospitalized. Two days later labor started spontaneously and a dead fetus was delivered normally. She underwent no operation and died twelve hours after delivery. Undoubtedly this was a case of intestinal obstruction, and operation should have been performed early. Persistent vomiting and abdominal pain in a patient who is pregnant and without symptoms of toxemia should be considered indicative of an acute abdomen. The only way to operate successfully on acute intestinal obstruction is to operate early. This patient did not receive the most intelligent treatment.

The second patient, who had had a previous cesarean section, was again delivered by section in her third pregnancy. She was known to have a hernia in the old scar, and following operation she had attacks of abdominal pain, nausea and vomiting, for which Levine-tube treatment was instituted without relief. Death occurred on the fifth post-partum day, and autopsy revealed incarcerated loops of small intestine in the hernia. There is no excuse for this fatality. The diagnosis of intestinal obstruction should have been made earlier, and immediate operation should have been performed.

Of the third case in this group the history is inadequate. The patient was apparently delivered normally but died from peritonitis following intestinal obstruction, which was due to gangrene of the rectum.

Of the 2 deaths associated with ovarian cyst, the first occurred in a patient who was hospitalized because of evidence of salpingitis; in spite of a spiking temperature and a white-cell count of 24,000 she left the hospital against advice. Operation was performed one month later because of continued pain; a pyosalpinx was discovered, and considerable pus was evacuated. A right ovarian cyst was also found, which ruptured on attempted removal. In addition, there was a three to four months' pregnancy, which had not been suspected. Death occurred from peritonitis. Pregnancy occurring in a patient suffering from acute salpingitis is certainly very unusual. It is probable that, had the salpingitis been treated conservatively and operation deferred, this fatality would not have taken place.

The second patient, who was curetted for a spontaneous abortion at about two months, developed sudden pain in the abdomen as she was about to be discharged from the hospital. Immediate operation revealed internal abdominal hemorrhage. It is said that the hemorrhage came from a ruptured ovarian cyst on the right. The patient died within thirty-six hours of the operation from continued bleeding associated with oozing from the abdominal wall. It is probable that a ruptured ectopic pregnancy was the cause of the intra-abdominal bleeding.

The chief lesson to be deduced from these surgical deaths is, Pregnancy should never be allowed to obscure a proper diagnosis. Consultation should be held in any questionable case of abdominal symptomatology. Early diagnosis means early operation; early operation, in contrast to deferred operation, means recovery rather than fatality. The patient who is reported to have had salpingitis should in all probability never have been operated on. The questionable case of ruptured extra-uterine pregnancy represents a fatality due to incorrect diagnosis.

SECRETARY'S OFFICE

The following letter appears to be of sufficient general interest and importance to warrant publication.

MICHAEL A. TIGHE, *Secretary*

* * *

Dear Dr. Tighe:

During the next twelve months 276 nurses are to be drawn from New England every month to enter the military services, which means that a total of 3312 nurses under forty years of age will be lost from our civilian services in this area by the end of the year; 140 a month will be drawn from Massachusetts alone. This is a large number, and in order to reach it, almost every eligible nurse who can possibly go will have to volunteer. If we can retain enough young instructors and supervisors to keep up the preparation of new nurses, we shall be very fortunate. For almost every other position, the nurses ineligible for military service will have to fill in. The understanding and support of physicians in encouraging the eligible young nurse to answer the call (which is still voluntary) is much needed.

This will leave many vacancies in hospitals to be filled by *increased classes of student nurses*, which is one of the essential ways of keeping up hospital standards of care. Recruitment of student nurses for schools of nursing grows constantly more difficult, in competition with the WAVES and WAACs and well-paying industrial jobs. Our midyear (February, 1943) classes in Massachusetts alone need 1100 more applicants to meet the quotas set. Connecticut needs 351; Rhode Island 71; Maine 302; New Hampshire 148; Vermont 127; according to quotas.

The supply of student nurses is the concern of physicians as well as nurses. Studies have shown that family physicians have marked influence in directing young women toward nursing as a career. That is why we are

addressing this letter to you, hoping that it may reach many physicians who will give this campaign for student nurses their active support.

Several questions are inevitable, which the following may answer:

1. *Where can the applicant find out about accredited schools of nursing?*

From the secretary of the state Nursing Council for War Service: in Massachusetts at 420 Boylston Street, Boston; in Connecticut at 252 Asylum Street, Hartford; in Rhode Island at 42 Weybosset Street, Providence; in Maine at 54 Saunders Street, Portland; in New Hampshire at Elliot Community Hospital, Keene; and in Vermont at 3 Nelson Street, Montpelier.

2. *What are the requirements for entrance?*

A high-school diploma with better than medium grades in the academic or college-preparatory course, with a minimum age of eighteen years. Married students are now accepted in most schools.

3. *What are resources for financial aid for those unable to meet the costs of a three-year course?*

The federal government has appropriated \$3,500,000 for nursing education, part of which is available for scholarships to cover tuition and entrance expenses, uniforms, books and so forth. This fund is available to accredited schools of nursing in hospitals with daily averages of 90 to 100 patients, or to smaller schools affiliating with others to make a well-rounded course. Tuition costs range from nothing to several hundred dollars, but the average is \$75.00.

The Federation of Women's Clubs in all the states are undertaking aid to student nurses as one of their year's activities and will have scholarship funds for personal expenses for students.

Both these funds are assigned through the directors of the schools of nursing, to whom the students should apply.

Some schools will concentrate the instruction in the first two and a half years of training, paying the students for their services during the last six months.

4. *What is the future for these student nurses who now crowd the schools of nursing?*

New positions will inevitably be available in the Army and Navy Nurse Corps after the war, if larger military forces are maintained, as seems likely. Greatly increased numbers will be needed in veterans' services.

The field of public health, both in this country and in reconstruction in other lands, is due for expansion. Hospitals will again replace students with graduates after the war. Marriage will take its usual toll. The opportunities for the well-qualified nurse seem to be broadening. Some unemployment of the poorly equipped nurse will probably be unavoidable.

5. *What resources are available for the hospital that has no room for enlarged classes of student nurses?*

The federal fund of \$3,500,000 is available for extra subsistence, including housing, food and laun-

dry, for additional instructors and instructional facilities and for expansion of clinical experience through affiliation with other institutions. Hospitals with daily averages of 90 to 100 patients may qualify. Smaller ones may qualify through affiliation with other institutions and centralization of instructional facilities to form a well rounded modern unit for nursing education. Application should be made to the United States Public Health Service. Full details have been sent to every hospital.

These are the facts. We need the co-operation of physicians in helping nursing to meet the demands of the military services for graduates, and the requirements of the hospitals for new students.

Yours very truly,

HELENE G. LEE, *Executive Secretary*
Massachusetts Nursing Council for War Service

-20 Boylston Street
Boston

WAR ACTIVITIES

CIVILIAN DEFENSE

PLANS FOR MORTUARY SERVICE

The Medical Division of the United States Office of Civilian Defense has issued *Medical Division Bulletin No. 5, Emergency Mortuary Services*, presenting plans for the organization of this essential part of the casualty services.

The bulletin suggests that the local chief of Emergency Medical Service, in co-operation with the medical examiner or coroner, the chief of police, the health officer and representatives of the private funeral directors and cemeteries, plan for the following necessary services: location of morgue facilities, administration of these facilities, training of supplementary mortuary personnel, responsibility for collection and preparation of the dead for burial rules for emergency issuance of death certificates and burial permits, types of inquests, if any, to be required, safeguarding of personal property of the dead, manufacture of board coffins, pooling of equipment and personnel of private mortuaries in emergencies, identification procedures, burial places for unclaimed and unidentified bodies, preparation of mortality lists, and arrangements with adjacent communities for mutual aid.

Morgue facilities should include a main morgue, usually the community's public morgue, and supplementary morgues as necessary to provide space for bodies in a ratio of 2 per 1000 population in target areas. Skating rinks, gymnasiums, auditoriums and similar buildings are suggested.

The staff of the Emergency Mortuary Service as set out in the bulletin includes a physician to confirm deaths. Other members of the staff are the director, recorder, property officer, identification officer, coroner's or medical examiner's representative, morgue attendants, clerical assistants and receptionists.

It is recommended that the identification tags used in the field casualty service for wounded be attached also to the dead in the field. Whenever possible a physician should examine bodies before they are removed to a morgue, so that if there is doubt of death in any case, the body may be taken to a casualty station or hospital for observation.

The bulletin outlines procedures for the reception of bodies at the morgue, the handling of personal property,

the storage of bodies, identification and the release and disposal of bodies. Special measures for the handling of gas contaminated bodies are described.

Federal funds are available under certain conditions pay funeral and cemetery expenses. Mass disposal of bodies, either by burial in a common grave or by cremation should be used only in the event of extremely large numbers of casualties which overwhelm regular and emergency mortuary facilities, and create a public health menace.

The bulletin deals briefly with the reporting of casualties and recommends that information be released direct to the Casualty Information Service. Plans are also presented for the safeguarding of valuables and for the collection and storage of the morgue records.

MISCELLANY

DR. WILINSKY'S SIXTIETH BIRTHDAY

On Sunday, December 20, approximately three hundred and fifty persons assembled at the Nurses' Home of Beth Israel Hospital to honor the sixtieth birthday of Dr. Charles F. Wilinsky. The speakers included Judge A. Mrs. Abraham E. Pinanski, Judge A. K. Cohen, James Hamilton, president of the American Hospital Association, and Dr. Samuel A. Robins. Dr. Wilinsky presented with a handsomely bound volume containing several hundred congratulatory letters from his friends, various parts of the country, several checks of appreciation for the use of the Beth Israel Hospital and a portrait painted by Jacob Binder.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1942

DISEASE	OCTOBER 1942	OCTOBER 1941	FIVE YEAR AVERAGE
Anterior or polio myelitis	7	46	19
Chicken pox	291	571	415
Diphtheria	13	8	15
Dog bite	842	857	806
Dysentery, bacillary	315	43	50
German measles	58	35	27
Gonorrhea	384	351	412
Measles	541	373	321
Meningitis men. meningococcal	12	8	6
Meningitis other forms	3	3	1
Mumps	401	335	397
Paratyphoid infection	13	6	3
Pneumonia lobar	242	192	222
Scarlet fever	622	466	312
Syphilis	610	450	425
Tuberculosis pulmonary	265	289	245
Tuberculosis other forms	13	29	31
Typhoid fever	7	11	7
Undulant fever	6	6	4
Whooping cough	737	555	468

*Based on figures for preceding five years.

†) Infectious meningitis only other forms reportable previous to 1915.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Braintree, Easton, 1, Fitchburg, 1, Fort Devens, 1, Salem, 1, Waltham, 1, Weymouth, 1, total, 7.

Diphtheria was reported from Billerica, 1, Blackstone, 1, Boston, 2, Fall River, 4, Lowell, 2, Springfield, Taunton, 1, West Brookfield, 1, total, 13.

Dysentery, bacillary, was reported from Lynn, 3, Quincy, 1, Salem, 1, Wrentham (State School), 309, total, 31.

Encephalitis, infectious, was reported from Everett, Somerville, 1, total, 2.

Meningitis, meningococcal, was reported from Boston, 2, Cambridge, 1, Cambridge, 2, Dracut, 1, Everett, 1.

Fall River, 1; Fitchburg, 1; Lowell, 1; Revere, 1; Woburn, 1; total, 12.

Meningitis, other forms, was reported from: Athol, 1; Boston, 1; Holyoke, 1; total, 3.

Paratyphoid infection was reported from: Boston, 2; Malden, 1; Norwood, 1; Quincy, 2; Somerville, 2; Southbridge, 1; West Boylston, 4; total, 13.

Septic sore throat was reported from: Boston, 6; Brockton, 1; Cambridge, 2; Winchester, 2; total, 11.

Trichinosis was reported from: New Bedford, 1; total, 1.

Typhoid fever was reported from: Becket, 5; Boston, 1; Milton, 1; total, 7.

Undulant fever was reported from: Danvers, 1; Gloucester, 1; Lexington, 1; Medford, 1; North Adams, 1; Whately, 1; total, 6.

Communicable diseases in general showed the usual seasonal increase.

Record-high figures were attained by mumps for the fourteenth time during the past sixteen months.

Whooping cough, German measles, paratyphoid infection, syphilis and bacillary dysentery were all reported at record-high figures. An outbreak in an institution is responsible for the high figures for bacillary dysentery.

Diseases reported at figures above their respective five-year averages were measles, meningococcal meningitis, lobar pneumonia, scarlet fever, dog bite, pulmonary tuberculosis and undulant fever.

The figure for typhoid fever was equal to the five-year average of the disease.

Reported at figures below their respective five-year averages were anterior poliomyelitis, chicken pox, diphtheria and gonorrhea.

Tuberculosis, other forms, was reported at a record low incidence.

Animal rabies was again reported from the focus previously mentioned in Norfolk County.

ARMY-NAVY "E" AWARD TO WINTHROP CHEMICAL COMPANY

On December 17, the Winthrop Chemical Company was presented the Army-Navy "E" award for its production of drugs essential to the war effort. The ceremonies were held in the morning at the plant in Rensselaer, New York, and in the evening at the Hotel New Yorker, New York City, for the employees in that city. Dr. Morris Fishbein was principal speaker at both occasions, and Brigadier General Charles C. Hillman and Rear Admiral Charles S. Stephenson made the award. Of the more than a hundred drugs being furnished by the Winthrop Chemical Company to the armed forces of the United Nations, the most important are Atabrine, Plasmochin, Naphuride, Avertin and the various sulfonamides.

NOTE

General Frederick F. Russell, professor of preventive medicine and epidemiology, emeritus, at Harvard Medical School, was recently awarded one of three William Crawford Gorgas medals by the Association of Military Surgeons of the United States. These medals and the attached honorariums have been made possible by a grant from John Wyeth and Brother, Incorporated, of Philadelphia, and the award to General Russell was based on his pioneer work in immunization against typhoid fever. The other recipients were Rear Admiral Edward R. Stitt and Brigadier General Jefferson R. Kean.

BOOK REVIEWS

Gynecology and Female Endocrinology. By Emil Novak, M.D., D.Sc. (hon., Dublin). 4°, cloth, 605 pp., with 11 illustrations. Boston: Little, Brown and Company, 1942. \$10.00.

The difference between this and earlier work on gynecology is clearly seen in the section on menstruation. It was only a few years ago that such a chapter was devoted to the anatomic description of what happened locally to the uterine wall. The present work tells a sequential story, which embodies endocrinology, physiology and anatomy, and the reader appreciates that he is beginning to get a view of what makes the wheels turn.

It is through the newer knowledge of endocrinology that a more rational approach can be made to both functional and organic disorders of the female generative tract. Dysmenorrhea, menorrhagia, sterility and habitual abortion are a few of the conditions in which the experimentalist has been helpful. In addition to presenting the latest innovations, the author also questions some of the traditional methods as experimental. For example, he states that the value of pregnant-mare serum in producing ovulation in women is still open to question. Busy clinicians require a sane evaluation such as this to overcome the obvious high-pressure methods of the commercial houses to push their products.

Because of the many new things in this book, one is likely to overlook the very excellent discussion on pathology, which is presented with the help of numerous illustrations, including some excellent colored plates.

Dr. Novak has written this book primarily for general practitioners and medical students, and operative technique has been deleted. The material has been judiciously selected, and the style of writing moves smoothly like a well-told story. The result is the finest work on gynecology in many years.

Solving School Health Problems: The Astoria demonstration study. Sponsored by the Department of Health and the Board of Education of New York City. By Dorothy Nyswander, Ph.D. 8°, cloth, 377 pp. New York: Commonwealth Fund, 1942. \$2.00.

This volume presents the details of a four-year study of school health services in New York City carried on during the period from 1936 to 1940. It outlines and discusses problems of administration, record forms, nurse's duties and opportunities, teacher's participation, dental care and tests for visual and for auditory acuity, including the presentation of many forms and blanks that have been found useful.

The following quotation gives an idea of the progress and outlook of the study as a whole: "Statistics of defects found and defects corrected furnish no index of school health problems which any individual child may develop later; they offer no index that the larger objectives of school health service are being reached; they give no evidence of the quality of work performed; they are not adapted to a single good supervisory technique which seeks to find out how to give better continuing supervision to individual children." This better-continuing supervision is dealt with in a positive way wherever possible.

The book is one of quality, and worthy of the care with which it has been printed and bound. It should be of interest to all school health administrators — physicians

